# $S_N^H$ reactions of pyrazine *N*-oxides and 1,2,4-triazine 4-oxides with CH-active compounds

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Nucleophilic substitution of hydrogen in pyrazine *N*-oxides under the action of CH-active compounds requires activation with acylating agents. This activation facilitates aromatization of intermediate $\sigma^H$ adducts *via* elimination of the acid residue to form substituted pyrazines. More electrophilic 1,2,4-triazine 4-oxides react with carbanions derived from CH-active compounds without additional activation according to a scheme, which has previously been unknown for azine *N*-oxides. This scheme involves aromatization of $\sigma^H$ adducts through elimination of water by the *E*1*cb* mechanism. The reaction products occur in DMSO-$d_6$ solutions predominantly as 6-methylene-1,6-dihydropyrazines and 5-methylene-4,5-dihydro-1,2,4-triazines.

**Key words:** nucleophilic substitution of hydrogen, 1,2,4-triazine 4-oxide, pyrazine 1-oxide, carbanion, CH-active compounds.

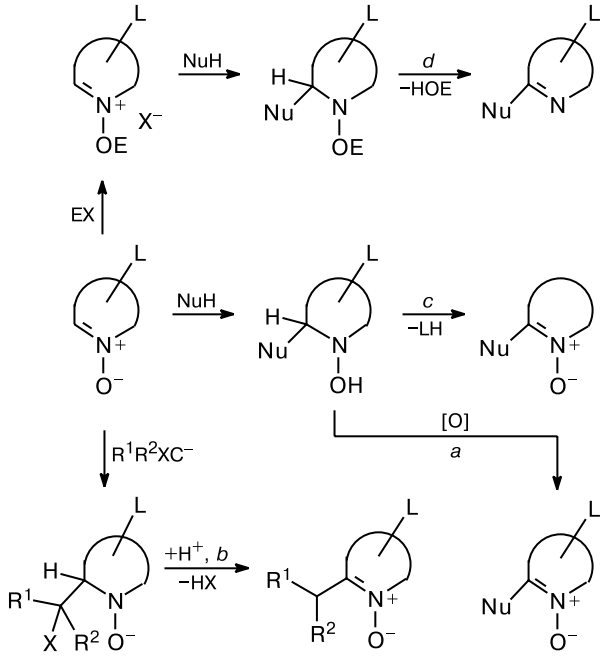
The nucleophilic substitution of hydrogen ($S_N^H$) in azine *N*-oxides involves two main steps, *viz.*, the addition of a nucleophile at the unsubstituted carbon atom of the heterocyclic system and aromatization of the resulting $\sigma^H$ adducts,[1,2] the latter reaction being generally the key step of the process. Since elimination of the $H^-$ ion, as such, is highly improbable, further transformations of $\sigma^H$ adducts involve their aromatization through oxidation or autoaromatization accompanied by *ipso*- or *tele*-elimination of the nucleofuge.

Oxidative aromatization of $\sigma^H$ adducts (Scheme 1, path *a*) takes place, for example, in the case of direct amination of pyridazine 1-oxides and 1,2,4-triazine 4-oxides,[3,4] reactions of 1,2,4-triazine 4-oxides with phenols[5] and indoles,[6] cyanation of quinoline 1-oxides,[7,8] and hydrolysis of 5,8-dimethyl-5,7(6*H*,8*H*)-dioxopyrimido[4,5-*e*][1,2,4]-triazine 4-oxide.[9]

Autoaromatization of $\sigma^H$ adducts does not require the presence of an external oxidizing agent, because the proton abstraction from the geminal center of $\sigma^H$ adducts proceeds with elimination of an auxiliary group. Three main types of autoaromatization can be distinguished depending on the mode of introduction of an auxiliary group into the $\sigma^H$ adduct.

The 1,2-elimination of HX can proceed in reactions performed with the use of nucleophiles bearing the nucleofuge group X. In these reactions, the hydrogen atom is eliminated from the substrate and the X group is removed from the nucleophile fragment (Scheme 1, path *b*).

**Scheme 1**




L, X are good leaving groups, E is R (Alk, Ar), RCO

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Such reactions are called[10] vicarious nucleophilic substitution. The reactions of quinoline 1-oxides or 3-methoxy-1,2,4-triazine 1-oxide with anions of halomethyl aryl sulfones[11,12] can serve as examples of such transformations in the series of azine *N*-oxides.

In *tele*-substitution reactions, aromatization of $\sigma^H$ adducts proceeds through elimination of the leaving group from the atom of the azine core separated from the site of nucleophilic attack by one or several bonds (Scheme 1, path *c*). The synthesis of 5-amino-1,2,4-triazine 4-oxides from 3-pyrrolidino-1,2,4-triazine 4-oxides[13] provides an example.

Finally, the presence of the *N*-oxide group makes it possible to carry out aromatization of $\sigma^H$ adducts *via* elimination of hydrogen together with an oxygen-containing fragment (Scheme 1, path *d*). As an example, we refer to the reactions of quinoline, pyrazine, and 1,2,4-triazine *N*-oxides with water or alcohols in the presence of acetic anhydride or benzoyl chloride.[14—16] In the presence of acylating agents, the reactions of pyridine, quinoline, and isoquinoline *N*-oxides with diethyl phosphite,[17] potassium cyanide,[18] cyanoacetic ester, malonic ester, nitroacetic ester, dimedone, oxazoline, thiazoline, rhodanine, Meldrum's acid, and barbituric acid[19,20] as well as cyanation of pyrazine *N*-oxides[21,22] proceed according to this scheme.

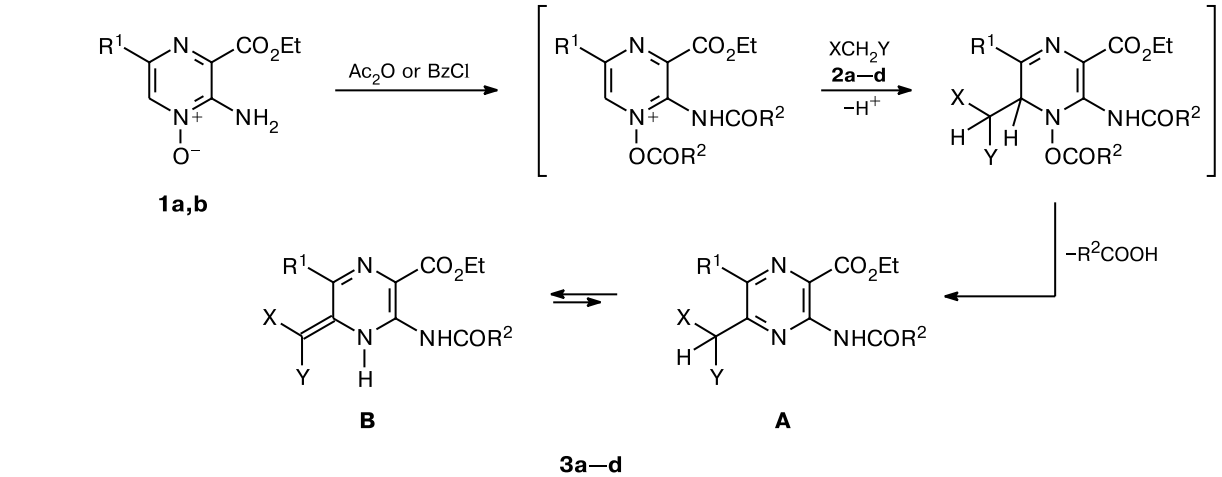
In the present study, we considered the $S_NH$ reactions of derivatives of pyrazine 1-oxide and 1,2,4-triazine 4-oxide with CH-active compounds. In spite of different conditions, all reactions proceed according to the general scheme of autoaromatization of $\sigma^H$ adducts.

## Results and Discussion

It was found that 2-amino-3-ethoxycarbonylpyrazine 1-oxides **1a,b** did not react with CH-active compounds or carbanions, which were generated from these compounds in the presence of bases, without additional activation. As expected, *O*-acyl pyrazinium salts used *in situ* appeared to be more reactive. Thus, pyrazine *N*-oxides **1a,b** were involved in the $S_NH$ reactions with malononitrile (**2a**), cyanoacetic ester (**2b**), indane-1,3-dione (**2c**), and barbituric acid (**2d**) in the presence of benzoyl chloride or acetic anhydride to give the corresponding 2-acylamino-3-ethoxycarbonyl-6-methylene-5-phenyl-1,6-dihydropyrazines **3a—d** (Scheme 2). The formation of *O*-acyl salts and acylation of the amino group activate pyrazine *N*-oxides **1a,b** with respect to the nucleophilic attack. Autoaromatization of intermediate $\sigma^H$ adducts acylated at the oxygen atom of the *N*-oxide group is facilitated due to elimination of the hydrogen atom, that is subjected to substitution, as the proton together with the anion of acetic or benzoic acid.

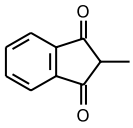
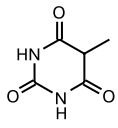
The presence of the additional nitrogen atom in 1,2,4-triazine 4-oxide promotes the nucleophilic substitution of hydrogen. In attempting to carry out the reactions with CH-active compounds without additional activation of the substrate, we discovered a new pathway of

**Scheme 2**




**1:** $R^1$ = Ph (**a**), Me (**b**)

$R^1$ = Ph, $R^2$ = Me (**3a,c**); $R^1$ = Me, $R^2$ = Ph (**3b**); $R^1$ = $R^2$ = Ph (**3d**)
X = Y = CN (**2a**, **3a**); X = CN, Y = $CO_2Et$ (**2b**, **3b**);

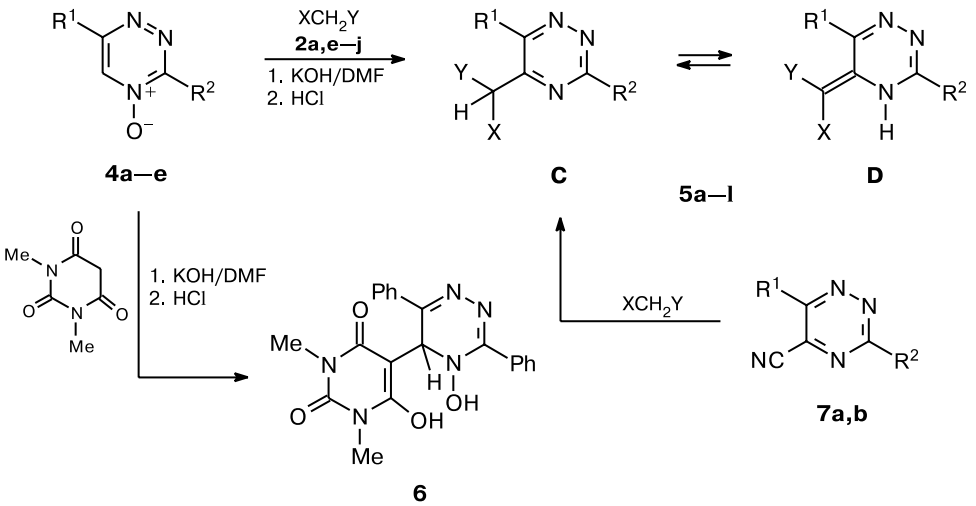
CHXY =  (**2c**, **3c**),  (**2d**, **3d**)

nucleophilic substitution of hydrogen, which has been unknown for azine *N*-oxides. Earlier,[23] we have reported the reactions of 3,6-diaryl-1,2,4-triazine 4-oxides with carbanions generated from certain CH-active compounds. In continuation of these studies, we found that 1,2,4-triazine 4-oxides **4a—e** react with malononitrile (**2a**), acetophenone (**2e**), 4-methylacetophenone (**2f**), 2-acetylthiophene (**2g**), phenylacetonitrile (**2h**), 4-chlorophenylacetonitrile (**2i**), and 2-thienylacetonitrile (**2j**) in a basic medium to give products of nucleophilic substitution of hydrogen, *viz.*, the corresponding 5-substituted 1,2,4-triazines **5a—k**. The reactions were accompanied by the loss of the *N*-oxide function (Scheme 3). The process is independent of the nature of substituents at positions 3 and 6 of the triazine ring but depends on the nature of the CH-active compound. The reaction of 1,2,4-triazine 4-oxide **4a** with 1,3-dimethylbarbituric acid in the presence of a base afforded only stable $\sigma^H$ adduct **6**, whereas autoaromatization products were not detected in this reaction.

Therefore, the highly electrophilic character of the 1,2,4-triazine ring makes it possible to perform the reaction without activation of the substrate, and the generation of the *N*-acyloxy- or *N*-alkoxy-1,2,4-triazinium cations is not needed.

The following mechanism may be proposed for the $S_NH$ reactions of 1,2,4-triazine 4-oxides **4** with carbanions. According to the commonly accepted concepts,[1] $S_NH$ reactions begin with the rapid reversible addition of a nucleophile at the unsubstituted carbon atom followed by slow aromatization of the resulting $\sigma^H$ adducts. Hence, it is reasonable to assume that the addition of a carbanion at position 5 of heterocycles **4** gives rise to anionic $\sigma^H$ adducts **E**. Due to the strong electron-withdrawing properties of the 1,2,4-triazine ring, the proton attached to the $sp^3$-hybridized carbon atom at position 5 is sufficiently labile even compared to the methine proton of a fragment of the CH-active compound. The migration of one of these protons to the oxygen atom gives rise to anions **F** and **G**, respectively (Scheme 4). The pathway of further transformations depends on the equilibrium between anions **E**, **F**, and **G**. Thus, anion **E** can undergo only oxidative aromatization ($-2e$, $-H^+$). By contrast, anion **F** can be subjected to autoaromatization with elimination of the $HO^-$ ion to form directly products of nucleophilic substitution of hydrogen. In this case, the transformation of the anionic $\sigma^H$ adduct is accompanied by dehydration by the *E*1*cb* mechanism. Most likely, the reaction under consideration proceeds according to this scheme. Anion **G** can be generated in reactions performed with the use of

**Scheme 3**




**2:** X = Y = CN (**a**); X = Bz, Y = H (**e**), X = *p*-TolCO, Y = H (**f**); X = 2-thenoyl, Y = H (**g**); X = Ph, Y = CN (**h**); X = *p*-$ClC_6H_4$, Y = CN (**i**); X = thienyl-2, Y = CN (**j**)

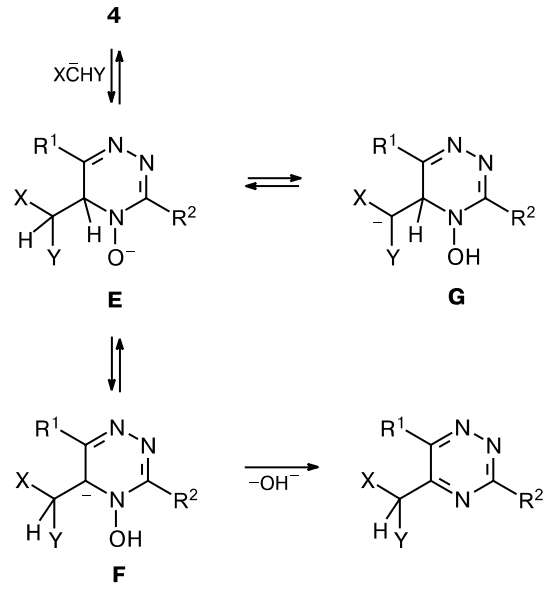
**4:** $R^1 = R^2$ = Ph (**a**); $R^1$ = Ph, $R^2$ = *p*-$ClC_6H_4$ (**b**); $R^1$ = *p*-$ClC_6H_4$, $R^2$ = Ph (**c**); $R^1$ = Ph, $R^2$ = furyl-2 (**d**); $R^1$ = *p*-$ClC_6H_4$, $R^2$ = furyl-2 (**e**)

| **5** | $R^1$ | $R^2$ | X | Y |
|---|---|---|---|---|
| **a** | Ph | Ph | Bz | H |
| **b** | Ph | Ph | *p*-TolCO | H |
| **c** | Ph | Ph | 2-thenoyl | H |
| **d** | *p*-$ClC_6H_4$ | 2-furyl | 2-thenoyl | H |
| **e** | Ph | Ph | CN | CN |
| **f** | Ph | *p*-$ClC_6H_4$ | CN | CN |
| **g** | Ph | Ph | Ph | CN |
| **h** | Ph | *p*-$ClC_6H_4$ | Ph | CN |
| **i** | *p*-$ClC_6H_4$ | Ph | Ph | CN |
| **j** | Ph | Ph | *p*-$ClC_6H_4$ | CN |
| **k** | *p*-$ClC_6H_4$ | Ph | *p*-$ClC_6H_4$ | CN |
| **l** | Ph | 2-furyl | 2-thienyl | CN |

**7:** $R^1 = R^2$ = Ph (**a**); $R^1$ = Ph, $R^2$ = *p*-$ClC_6H_4$ (**b**)

CH-active compounds possessing strong acidic properties and aromatization of this anion is also hindered. That is the reason why the reaction of 1,2,4-triazine 4-oxide with dimethylbarbituric acid ceased at the step of formation of the $\sigma^H$ adduct.

**Scheme 4**



The above-considered mechanism of autoaromatization of $\sigma^H$ adducts is supported by the formation of 5-cyano-1,2,4-triazines[25] and 5-cyanamido-1,2,4-triazines[26] in the $S_N^H$ reactions of 1,2,4-triazine 4-oxides **4** with cyanide anions as well as with cyanamide under basic conditions. In these processes, the fragment introduced by the nucleophile possesses strong electron-withdrawing properties, which enhances the mobility of the proton in the $\sigma^H$ adduct of type **E** (see Scheme 4) and, consequently, facilitates aromatization of the latter according to the proposed mechanism.

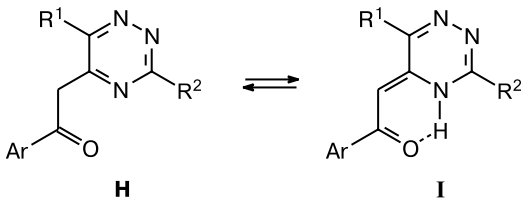
The $S_N^H$ reactions of azine *N*-oxides can proceed by the above-considered mechanism only if the proton in the $\sigma^H$ adduct is characterized by sufficiently high mobility, which is substantially influenced by the electron-withdrawing properties of the heterocycle. As was demonstrated above, pyrazine *N*-oxides do not react with carbanions without additional activation. In the series of mono- and diazines, the $\sigma^H$ adduct is insufficiently stabilized as an anion of type **F** due to which quinoline *N*-oxides and phthalazine 2-oxides react with carbanions only according to the scheme of oxidative (see Scheme 1, path *a*)[7,8,27,28] or vicarious (path *b*)[11] nucleophilic substitution of hydrogen with retention of the *N*-oxide function.

The structures of compounds **3a—d**, **5**, and **6** were established based on the results of elemental analysis, $^1$H NMR spectroscopy, and mass spectrometry. The structures of 1,2,4-triazines **5a,e,f,h** were confirmed by the independent synthesis involving the replacement of the cyano group in 5-cyano-1,2,4-triazines **7a,b** by the malononitrile, phenylacetonitrile, or acetophenone residue according to a method described earlier.[24]

Two prototropically isomeric forms **A** and **B** (see Scheme 2) and **C** and **D** (see Scheme 3) can be proposed for products **3a—d** and **5a—l**, respectively. Substantial differences in the $^1$H NMR spectra of these two isomers (high-field signal for the methine proton of form **A** (**C**) and a low-field-signal for the proton of the NH group of form **B** (**D**)) allowed us to use this method for determining the isomer ratio in solutions. It was found that the equilibrium between two possible isomeric forms of pyrazines **3a—d** in DMSO-$d_6$ solutions is completely shifted to 1,6-dihydropyrazines **B** (see Scheme 2).

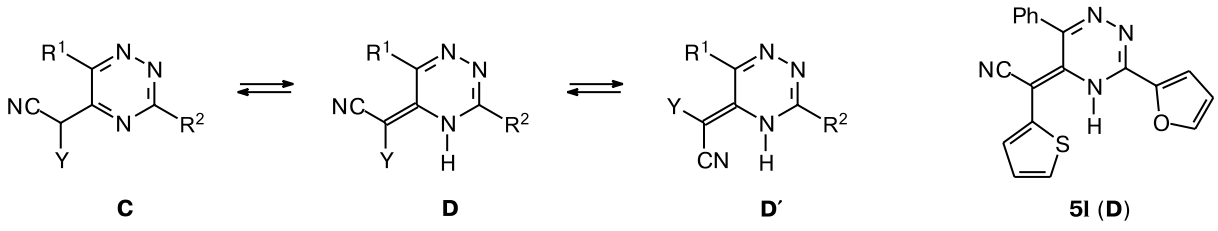
In DMSO-$d_6$ solutions, 1,2,4-triazines **5a—d** containing the ArCO group at position 5 of the heterocycle occur as 5-phenacyl-1,2,4-triazines **H** and 5-aroylmethylene-4,5-dihydro-1,2,4-triazines **I** (Scheme 5). The isomer ratio depends on the nature of substituents in 1,2,4-triazine, form **I** being most favorable. The latter form is, apparently, additionally stabilized by an intramolecular hydrogen bond.

**Scheme 5**



The introduction of the arylacetonitrile fragment into the 1,2,4-triazine molecule results in the fact that compounds **5e—k** in DMSO-$d_6$ occur exclusively as 5-cyanomethylene-4,5-dihydro-1,2,4-triazines **D**. This phenomenon has also been observed earlier[13] for 5-cyanomethyl-1,2,4-triazines. However, a double set of signals for the protons of the aryl substituents suggests the possible existence of 1,2,4-triazines **5g—k** as two *E* and *Z* isomers **D** and **D´** with respect to the exocyclic C=C bond (Scheme 6). By contrast, the product of the reaction of 1,2,4-triazine 4-oxide **1d** with 2-cyanomethylthiophene **2j**, *viz.*, 5-(α-cyano-α-thienyl-2-methylene)-3,6-diphenyl-4,5-dihydro-1,2,4-triazine (**5l**), occurs in a DMSO-$d_6$ solution as one isomer (**D**). It can be assumed that the additional Coulomb interaction between the S atom and the H atom of the triazine ring stabilizes *Z* isomer **5l** (**D**). The further assignment of the signals in the NMR spectra to a particular isomer was made by comparing them with the spectrum of compound **5l** (**D**).

**Scheme 6**




**C** **D** **D′** **5l (D)**

This enabled us to distinguish the signals of aromatic substituents in the 1,2,4-triazine ring corresponding to isomer **D**. This is particularly valid for the substituent $R^1$ at position 6 of the 1,2,4-triazine ring and the aromatic moiety of the nucleophilic fragment for which the proton signals should change most substantially on going from one isomer to another because these substituents in form **D** are in close proximity. Due to the mutual anisotropic influence of two benzene rings, the signals for the protons of these fragments in the $^1$H NMR spectra are shifted upfield. The characteristic signals revealed for forms **D** and **D′** allowed us to determine the isomer ratio by comparing the integral intensities of the corresponding protons. Analysis of the spectra demonstrated that the composition of the mixture depends on the nature of substituents, primarily, of the aromatic substituent in the nucleophilic fragment. For example, the introduction of the chlorine atom at the *para* position of the latter substituent increases steric hindrances to the formation of isomer **D′** thus decreasing its proportion in the mixture of two forms.

Therefore, the nucleophilic substitution of hydrogen in azine *N*-oxides with anionic nucleophiles can proceed with autoaromatization of intermediate $\sigma^H$ adducts *via* formal elimination of water by the *E*1*cb* mechanism. In these processes, the electron-withdrawing properties of the heterocycle play a decisive role.

## Experimental

The $^1$H NMR spectra were recorded on a Bruker WM-250 spectrometer (250.1 MHz) using DMSO-$d_6$ as the solvent (unless otherwise indicated) with $Me_4Si$ as the internal standard. The signals belonging to forms **C**, **D**, and **D′** are labeled by the corresponding indices (see Scheme 6). The mass spectra were obtained on a Varian MAT-311A instrument (electron beam ionization); the energy of ionizing electrons was 70 eV; direct inlet of samples. The course of the reactions and purities of the products were monitored by TLC on Silufol UV-254 plates using ethyl acetate as the eluent; visualization was carried out with UV light.

The commercial CH-active compounds were used as nucleophiles. Heterocyclic substrates, *viz.*, pyrazine 1-oxides **1**,[28] 1,2,4-triazine 4-oxides **4**,[29] and 5-cyano-1,2,4-triazines **7**,[24] were synthesized according to known procedures.

**2-Acetylamino-6-dicyanomethylene-3-ethoxycarbonyl-5-phenyl-1,6-dihydropyrazine (3a).** Pyrazine 1-oxide **1a** (520 mg, 2 mmol) and malononitrile (72 mg, 2 mmol) were dissolved in $Ac_2O$ (5 mL). Then $Et_3N$ (0.8 mL, 6 mmol) was added. The reaction mixture was kept at ~20 °C for 24 h and concentrated *in vacuo*. The residue was recrystallized from benzene. The yield was 260 mg (37%), m.p. 205 °C. $^1$H NMR, δ: 1.25 (t, 3 H, $CH_2C\underline{H}_3$); 2.41 (s, 3 H, $COC\underline{H}_3$); 4.22 (q, 2 H, $C\underline{H}_2CH_3$); 7.34—7.41 (m, 5 H, Ph); 10.52 (s, 1 H, NHAc). MS, *m/z* ($I_{rel}$ (%)): 349 $[M]^+$ (100). Found (%): C, 61.74; H, 4.40. $C_{18}H_{15}N_5O_3$ (349.4). Calculated (%): C, 61.89; H, 4.33.

**2-Benzoylamino-6-cyano(ethoxycarbonyl)methylene-3-ethoxycarbonyl-5-methyl-1,6-dihydropyrazine (3b).** Pyrazine 1-oxide **1b** (395 mg, 2 mmol) and ethyl cyanoacetate **2b** (0.21 mL, 2 mmol) were dissolved in DMF (5 mL). Then benzoyl chloride (1.2 mL, 10 mmol) was added and the reaction mixture was heated at 100 °C for 1 h. The precipitate that formed was filtered off and recrystallized from DMF. The yield was 317 mg (40%), m.p. 237 °C. $^1$H NMR, δ: 1.34 and 1.40 (both t, 3 H each); 2.73 (s, 3 H, 5-Me); 4.30 (q, 2 H); 4.40 (q, 2 H); 7.60—7.99 (m, 5 H, Ph); 12.50 (s, 1 H, NHBz); 15.85 (s, 1 H, 1-NH). MS, *m/z* ($I_{rel}$ (%)): 396 $[M]^+$ (100). Found (%): C, 60.55; H, 5.24; N, 14.21. $C_{20}H_{20}N_4O_5$ (396.4). Calculated (%): C, 60.60; H, 5.09; N, 14.13.

**2-Acetylamino-6-(1,3-dioxoindan-2-ylidene)-3-ethoxycarbonyl-5-phenyl-1,6-dihydropyrazine (3c).** Pyrazine 1-oxide **1a** (780 mg, 3 mmol) and 1,3-indanedione **3** (438 mg, 3 mmol) were dissolved in $CF_3COOH$ (3 mL) and then $Ac_2O$ (1 mL) was added. The reaction mixture was kept for 24 h. The precipitate that formed was filtered off and recrystallized from toluene. The yield was 760 mg (59%), m.p. >250 °C. $^1$H NMR ($CDCl_3$), δ: 1.44 (t, 3 H, $CH_2C\underline{H}_3$); 2.39 (s, 3 H, $C\underline{H}_3CO$); 4.42 (q, 2 H, $C\underline{H}_2CH_3$); 7.37—7.66 (m, 9 H, H arom.); 11.62 (s, 1 H, $N\underline{H}Ac$); 16.25 (br.s, 1 H, H(1)). MS, *m/z* ($I_{rel}$ (%)): 429 $[M]^+$ (100). Found (%): C, 67.30; H, 4.28; N, 9.73. $C_{24}H_{19}N_3O_5$ (429.4). Calculated (%): C, 67.13; H, 4.46; N, 9.78.

**2-Benzoylamino-3-ethoxycarbonyl-5-phenyl-6-(2,4,6-trioxopyrimidin-5-ylidene)-1,6-dihydropyrazine (3d).** Pyrazine 1-oxide **1a** (500 mg, 1.93 mmol) and benzoyl chloride (1 mL) were added to a suspension of sodium barbiturate (900 mg, 6 mmol) in DMF (10 mL). The reaction mixture was heated for 1 h, diluted with water, and neutralized with a 25% $NH_3$ solution to pH 7. The precipitate that formed was filtered off, washed with water, and recrystallized from aqueous AcOH. The yield was 330 mg (36%), m.p. 250 °C. $^1$H NMR, δ: 1.36 (t, 3 H, $CH_2C\underline{H}_3$); 4.39 (q, 2 H, $C\underline{H}_2CH_3$); 7.32—8.05 (m, 10 H, H arom.); 10.99—11.80 (br.s, 3 H, 3 NH). MS, *m/z* ($I_{rel}$ (%)): 473 $[M]^+$ (43). Found (%): C, 60.81; H, 4.16. $C_{24}H_{19}N_5O_6$ (473.5). Calculated (%): C, 60.89; H, 4.05.

**Reactions of 1,2,4-triazine 4-oxides 4 with CH-active compounds 2a,e—j (general procedure).** The corresponding precur-

sor of the carbanion (1.1 mmol) and then 1,2,4-triazine 4-oxide **4** (1 mmol) were added to a suspension of triturated KOH (500 mg) in DMF (3 mL). The reaction mixture was stirred at ~20 °C for 1—5 h, diluted with water, and acidified with dilute HCl to pH 3. The precipitate that formed was filtered off and recrystallized from EtOH or AcOH.

**Synthesis of 1,2,4-triazines 5a,e,f,h by the reactions of 5-cyano-1,2,4-triazines 7a,b with CH-active compounds 2a,e,h.** Compound **2a,e,h** (1.05 mmol) was added with stirring to a 60% NaH suspension in mineral oil (45 mg, 1.1 mmol of NaH) in THF (4 mL). After 15 min, the corresponding 5-cyano-1,2,4-triazine **7a,b** (1.0 mmol) was added. The reaction mixture was stirred at ~20 °C for 2 h. The solvent was evaporated *in vacuo*. The residue was dissolved in water and acidified with dilute HCl to pH 3. The precipitate that formed was filtered off and recrystallized from EtOH.

**5-Phenacyl-3,6-diphenyl-1,2,4-triazine (5a).** The yield was 160 mg (45%), m.p. 194—196 °C (192—194 °C, *cf.* lit. data[23]). $^1$H NMR, δ: 4.74$^{C}$ (s, 0.4 H, $CH_2$); 6.32$^{D}$ (s, 0.8 H, CH); 7.40—7.95 (m, 13 H); 8.31$^{D}$ (m, 1.6 H); 8.46$^{C}$ (m, 0.4 H); 15.7$^{D}$ (br.s, 0.8 H, NH). Found (%): C, 78.49; H, 4.75; N, 12.20. $C_{23}H_{17}N_3O$ (351.4). Calculated (%): C, 78.61; H, 4.88; N, 11.96.

**3,6-Diphenyl-5-(*p*-toluoyl)methyl-1,2,4-triazine (5b).** The yield was 145 mg (40%), m.p. 183—185 °C. $^1$H NMR, δ: 2.40$^{D}$ (s, 2.55 H, Me); 2.42$^{C}$ (s, 0.45 H, Me); 6.32$^{C}$ (s, 0.85 H, CH); 4.70$^{C}$ (s, 0.30 H, $CH_2$); 7.25 (m, 2 H); 7.40—7.85 (m, 10 H); 8.32$^{D}$ (m, 1.7 H); 8.46$^{C}$ (m, 0.3 H); 15.6$^{D}$ (br.s, 0.85 H, NH). Found (%): C, 79.01; H, 5.33; N, 11.72. $C_{24}H_{19}N_3O$ (365.4). Calculated (%): C, 78.88; H, 5.24; N, 11.50.

**3,6-Diphenyl-5-(2-thenoyl)methyl-1,2,4-triazine (5c).** The yield was 240 mg (67%), m.p. 180—183 °C. $^1$H NMR, δ: 4.68$^{C}$ (s, 0.7 H, $CH_2$); 6.16$^{D}$ (s, 0.65 H, CH); 7.14$^{D}$ (dd, 0.65 H, $J$ = 4.8 and 4.0 Hz); 7.20$^{C}$ (dd, 0.35 H, $J$ = 4.8 and 4.1 Hz); 7.56$^{D}$ (dd, 0.65 H, $J$ = 4.8 and 0.9 Hz); 7.78$^{D}$ (dd, 0.65 H, $J$ = 4.0 and 0.9 Hz); 7.94$^{C}$ (dd, 0.35 H, $J$ = 4.8 and 1.1 Hz); 7.96$^{C}$ (dd, 0.35 H, $J$ = 4.1 and 1.1 Hz); 8.23$^{D}$ (m, 1.3 H); 8.45$^{C}$ (m, 0.7 H); 15.6$^{D}$ (br.s, 0.65 H, NH). Found (%): C, 70.41; H, 4.30; N, 11.93. $C_{21}H_{15}N_3OS$ (357.4). Calculated (%): C, 70.57; H, 4.23; N, 11.76.

**6-(4-Chlorophenyl)-3-(2-furyl)-5-(2-thenoyl)methyl-1,2,4-triazine (5d).** The yield was 225 mg (59%), m.p. 203—205 °C. $^1$H NMR, δ: 4.66$^{C}$ (s, 0.4 H, $CH_2$); 6.15$^{D}$ (s, 0.8 H, CH); 6.71$^{C}$ (dd, 0.2 H, $J$ = 3.0 and 1.1 Hz); 6.79 (dd, 1 H, $J$ = 3.0 and 1.0 Hz); 7.13$^{D}$ (dd, 1 H, $J$ = 4.9 and 4.0 Hz); 7.20$^{C}$ (dd, 0.2 H, $J$ = 4.9 and 4.0 Hz); 7.31$^{C}$ (m, 0.4 H); 7.38$^{D}$ (m, 1.6 H); 7.42$^{C}$ (d, 0.2 H, $J$ = 3.0 Hz); 7.48 (d, 1 H, $J$ = 3.0 Hz); 7.50—7.62 (m, 2.8 H); 7.76$^{D}$ (dd, 1 H, $J$ = 4.0 and 1.0 Hz); 7.91$^{C}$ (d, 0.2 H, $J$ = 1.1 Hz); 7.93$^{C}$ (dd, 0.2 H, $J$ = 4.9 and 1.0 Hz); 7.95$^{C}$ (dd, 0.2 H, $J$ = 4.0 and 1.0 Hz); 8.39 (d, 1 H, $J$ = 1.0 Hz); 15.3$^{D}$ (br.s, 0.8 H, NH). Found (%): C, 59.61; H, 3.34; N, 11.17. $C_{19}H_{12}ClN_3O_2S$ (381.8). Calculated (%): C, 59.77; H, 3.17; N, 11.00.

**5-Dicyanomethylene-3,6-diphenyl-4,5-dihydro-1,2,4-triazine (5e).** The yield was 160 mg (54%), m.p. 264—267 °C (decomp.). $^1$H BNR, δ: 6.88—6.92$^{D'}$ (m, 2.0 H, Ph); 7.00$^{D'}$ and 7.24$^{D'}$ (both m, 1.2 H and 0.8 H, 6-Ph); 7.32—7.62 (m, 6.8 H); 7.68$^{D'}$ (m, 1.2 H); 8.04$^{D}$ (m, 1.2 H); 8.20$^{D'}$ (m, 0.8 H); 13.3 (br.s, 1 H); 7.45 (m, 3 H); 7.62 (m, 2 H); 7.72 (m, 3 H); 8.19 (m, 2 H); 14.9 (br.s, 1 H, NH). Found (%): C, 72.81; H, 3.58; N, 23.71. $C_{18}H_{11}N_5$ (297.3). Calculated (%): C, 72.72; H, 3.73; N, 23.55. MS, $m/z$ ($I_{rel}$ (%)): 297 $[M]^+$ (87).

**3-(4-Chlorophenyl)-5-dicyanomethylene-6-phenyl-4,5-dihydro-1,2,4-triazine (5f).** The yield was 210 mg (63%), m.p. >270 °C. $^1$H NMR, δ: 7.40—7.60 (m, 5 H); 7.65 (m, 2 H); 8.20 (m, 2 H); 14.8 (br.s, 1 H, NH). Found (%): C, 65.21; H, 3.15; N, 21.00. $C_{18}H_{10}ClN_5$ (331.7). Calculated (%): C, 65.17; H, 3.04; N, 21.11. MS, $m/z$ ($I_{rel}$ (%)): 333 $[M]^+$ (28) and 331 $[M]^+$ (81).

**5-Cyano(phenyl)methylene-3,6-diphenyl-4,5-dihydro-1,2,4-triazine (5g).** The yield was 300 mg (86%), m.p. 256 °C. $^1$H NMR, δ: 6.90$^{D'}$ (br.s, 2.25 H, Ph); 6.90—7.10$^{D'}$ (m, 1.35 H, 6-Ph); 7.20—7.70 (m, 8.1 H, arom.$^{D,D'}$); 7.88$^{D}$ (m, 1.1 H); 8.02$^{D}$ (m, 1.1 H); 8.2$^{D'}$ (m, 0.9 H); 13.4 (br.s, 1 H, NH). Found (%): C, 79.41; H, 4.66; N, 15.91. $C_{23}H_{16}N_4$ (348.4). Calculated (%): C, 79.29; H, 4.63; N, 16.08. MS, $m/z$ ($I_{rel}$ (%)): 348 $[M]^+$ (21).

**3-(4-Chlorophenyl)-5-cyano(phenyl)methylene-6-phenyl-4,5-dihydro-1,2,4-triazine (5h).** The yield was 350 mg (91%), m.p. >270 °C. $^1$H NMR, δ: 6.95$^{D'}$ (br.s, 2.25 H, Ph); 7.05$^{D'}$ and 7.23$^{D'}$ (both m, 1.35 H each, 6-Ph); 7.30$^{D}$ (m, 0.55 H); 7.41$^{D}$ (m, 1.1 H); 7.49$^{D}$ (m, 1.65 H); 7.62—7.76 (m, 3.1 H); 7.82$^{D}$ (m, 1.1 H); 8.01$^{D}$ (m, 1.1 H); 8.18$^{D'}$ (m, 0.9 H); 13.3 (br.s, 1 H, NH). Found (%): C, 72.21; H, 3.90; N, 14.78. $C_{23}H_{15}ClN_4$ (382.8). Calculated (%): C, 72.16; H, 3.95; N, 14.63. MS, $m/z$ ($I_{rel}$ (%)): 384 $[M]^+$ (6) and 382 $[M]^+$ (17).

**6-(4-Chlorophenyl)-5-cyano(phenyl)methylene-3-phenyl-4,5-dihydro-1,2,4-triazine (5i).** The yield was 325 mg (85%), m.p. >270 °C. $^1$H NMR, δ: 6.98$^{D'}$ (br.s, 2.25 H, Ph); 7.03$^{D'}$ and 7.22$^{D'}$ (both m, 0.9 H and 0.9 H, 4-$ClC_6H_4$); 7.30$^{D}$ (m, 0.55 H); 7.42$^{D}$ (m, 1.1 H); 7.52—7.68 (m, 5.2 H); 7.85$^{D}$ (m, 1.1 H); 8.04$^{D}$ (m, 1.1 H); 8.18$^{D'}$ (m, 0.9 H); 13.3 (br.s, 1 H, NH). Found (%): C, 72.05; H, 4.08; N, 14.58. $C_{23}H_{15}ClN_4$ (382.8). Calculated (%): C, 72.16; H, 3.95; N, 14.63. MS, $m/z$ ($I_{rel}$ (%)): 384 $[M]^+$ (8) and 382 $[M]^+$ (24).

**5-(4-Chlorophenyl)cyanomethylene-3,6-diphenyl-4,5-dihydro-1,2,4-triazine (5j).** The yield was 310 mg (81%), m.p. >270 °C. $^1$H NMR, δ: 6.90$^{D'}$ (br.s, 1.4 H, $ClC_6H_4$); 7.00—7.30$^{D'}$ (m, 1.75 H, 6-Ph); 7.39$^{D}$ (m, 1.3 H); 7.40—7.75 (m, 6.25 H); 7.90$^{D}$ (m, 1.3 H); 8.04$^{D'}$ (m, 1.3 H); 8.19$^{D'}$ (m, 0.7 H); 13.6 (br.s, 1 H, NH). Found (%): C, 71.82; H, 3.74; N, 14.71. $C_{23}H_{15}ClN_4$ (382.8). Calculated (%): C, 72.16; H, 3.95; N, 14.63.

**6-(4-Chlorophenyl)-5-(4-chlorophenyl)cyanomethylene-3-phenyl-4,5-dihydro-1,2,4-triazine (5k).** The yield was 370 mg (89%), m.p. >270 °C. $^1$H NMR, δ: 6.80$^{D'}$ and 7.10$^{D'}$ (both m, 0.7 H each, $ClC_6H_4$); 7.12$^{D'}$ and 7.21$^{D'}$ (both m, 0.7 H each, $ClC_6H_4$); 7.88$^{D}$ (m, 2 H); 8.01$^{D}$ (m, 1.3 H); 8.15$^{D'}$ (m, 0.7 H); 13.5 (br.s, 1 H, NH). Found (%): C, 66.07; H, 3.17; N, 13.49. $C_{23}H_{14}Cl_2N_4$ (417.3). Calculated (%): C, 66.20; H, 3.38; N, 13.43.

**5-Cyano(2-thienyl)methylene-3-furyl-6-phenyl-4,5-dihydro-1,2,4-triazine (5l).** The yield was 210 mg (61%), m.p. >270 °C. $^1$H NMR, δ: 6.87 (dd, 1 H, $J$ = 3.2 and 1.3 Hz); 7.08 (dd, 1 H, $J$ = 4.8 and 4.1 Hz); 7.21 (dd, 1 H, $J$ = 4.8 and 1.0 Hz); 7.48 (m, 3 H); 7.55 (dd, 1 H, $J$ = 4.1 and 1.0 Hz); 7.60 (d, 1 H, $J$ = 3.2 Hz); 7.63 (m, 2 H); 8.13 (d, 1 H, $J$ = 1.3 Hz); 13.6 (br.s, 1 H, NH). Found (%): C, 66.12; H, 3.56; N, 16.35. $C_{19}H_{12}N_4OS$ (344.4). Calculated (%): C, 66.26; H, 3.51; N, 16.27.

**4-Hydroxy-5-(6-hydroxy-1,3-dimethyl-2,4-dioxo(1*H*,3*H*)-pyrimidin-5-yl)-3,6-diphenyl-4,5-dihydro-1,2,4-triazine (6).** The yield was 760 mg (59%), m.p. >270 °C. $^1$H NMR, δ: 3.07 (s, 6 H, 2NMe); 6.34 (s, 1 H, H(5)); 7.32—8.06 (m, 10 H, 2Ph); 11.62 (br.s, 1 H, OH); 12.78 (br.s, 1 H, OH). Found (%):

C, 62.10; H, 4.85; N, 17.21. $C_{21}H_{19}N_5O_4$ (405.4). Calculated (%): C, 62.22; H, 4.72; N, 17.27.

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