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# TRANSYLIDATION OF 3-METHYL-PHENACYLPYRIDAZINIUM YLIDES WITH PHENYLISOCYANATE. INFLUENCE OF TRIETHYLAMONIUM CATION OVER PROTOTROPIC REARRANGEMENT***

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Monosubstituted 3-methyl-phenacylpyridazinium ylides when treated *in situ* with phenylisocyanate in the presence of triethylamine give an intermediate that undergoes a prototropic rearrangement to the final disubstituted ylides. In order to gain further insight into the mechanism corresponding to the influence of triethylamine, three possible pathways were investigated, in the absence of tertiary base, in the presence of triethylamine, and *via* triethylamonium bromide by-product. It was our hypothesis that the presence of triethylamine in reacting mixture is responsible for reaction to take place. Indeed, theoretical study at B3LYP level of computation indicated triethylamonium catalyst as particular effective in this reaction for prototropy. Theoretical findings are consistent with the experimental study results.

## INTRODUCTION

Cycloimmonium ylides have formed an active area of chemical research because of either theoretical importance or their practical applications.[1] It has been shown that cycloiommonium ylides have interesting properties as analytical reagents[2] or semi-conducting materials[3] as well as biological active agents.[4] Moreover, as pyridazine derivatives, they are particularly effective for prophylaxis and treatment of various diseases.[5]

In the most cases, the ylides react as nucleophilic reagents as well as 1,3-dipoles in reaction with a large variety of dipolarophiles (with double or triple bonds) via a [3+2] dipolar cycloaddition.[6] Particularly, pyridazinium ylide with benzene afforded 1,3-cycloadducts.[7] It is well-known that cumulenes, in particular isocyanates, having a carbonyl group adjacent to the cumulative double bonds may react as dipolar reagents in cycloaddition reactions.[8] The addition of benzoyl isocyanate to phosphonium ylide having a hydrogen on the ylide carbon gave after proton migration the corresponding disubstituted phosphonium ylide, in good yields. Unlike the phosphonium ylide with an acyl group adjacent to the ylide carbon was reacted, the betaine was obtained in high yield, that in the further step decomposed easily to the starting compounds and the prototropic shift was no more observed.[9]

Recent studies on the reaction of disubstituted pyridinium ylides with aryl isocyanates and reversible migrations of alkoxycarbonyl groups from the ylide carbon to the nitrogen from isocyanate atom have been reported. In the first step an adduct is formed, that gives the carbamate final product by intramolecular rearrangement without formation of any cyclic intermediate compound.[10]

Some other authors have suggested the involvement of triethylamine used in deprotonation to the corresponding ylide of the imidazolium salts

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*** Dedicated to the memory of the great Man, Mircea Constantinescu

resulted in the reaction of 1-(N-imidazoyl)alkyl isocyanate with 1-chloro-alkyl isocyanate. Moreover, they considered that into the further step the intramolecular carbamoylation of ylide carbon atom occurs by the reaction of isocyanate group followed by the imidazole ring protonation with triethylammonium hydrochloride.[11]

These findings prompted us to investigate the transylidation mechanism of various monopyridazinium N-ylides with aryl isocyanates in the presence of triethylamine.

## RESULTS AND DISCUTION

In the first step a 3-methyl-phenacylpyridazinium ylides series was synthesized, that was further allowed to react *in situ* with phenylisocyanate when the corresponding disubstituted ylides resulted. Collaterally with the experimental work, a theoretical study at DFT level of theory was performed to determine the influence of triethylamine during transylidation of monoylides adduct with isocyanate to the correspondent final product.

### I. Synthetic approach

The synthesis of 3-methyl-phenacylpyridazinium salts series **1 (a-g)** was accomplished by the known Krohnke „salt metod"[12] from 3-methylpyridazine and different 4'-substituted bromoacetophenone, in benzene, at room temperature, as outlined in Scheme 1. The *in situ* treatment of the resulted salts solution with an excess of triethylamine afforded the monoylides **2 (a-g)** along triethylamonium bromide by-product as precipitate, easy removed by filtration. Monoylide transformation to the corresponding disubstituted 3-methyl-pyridazinum ylides **4 (a-g)** was accomplished easily by reacting with *p*-chlorophenyl isocyanate in benzene, at room temperature. These conditions easy leaded in 70-80% yields to the desired final product.

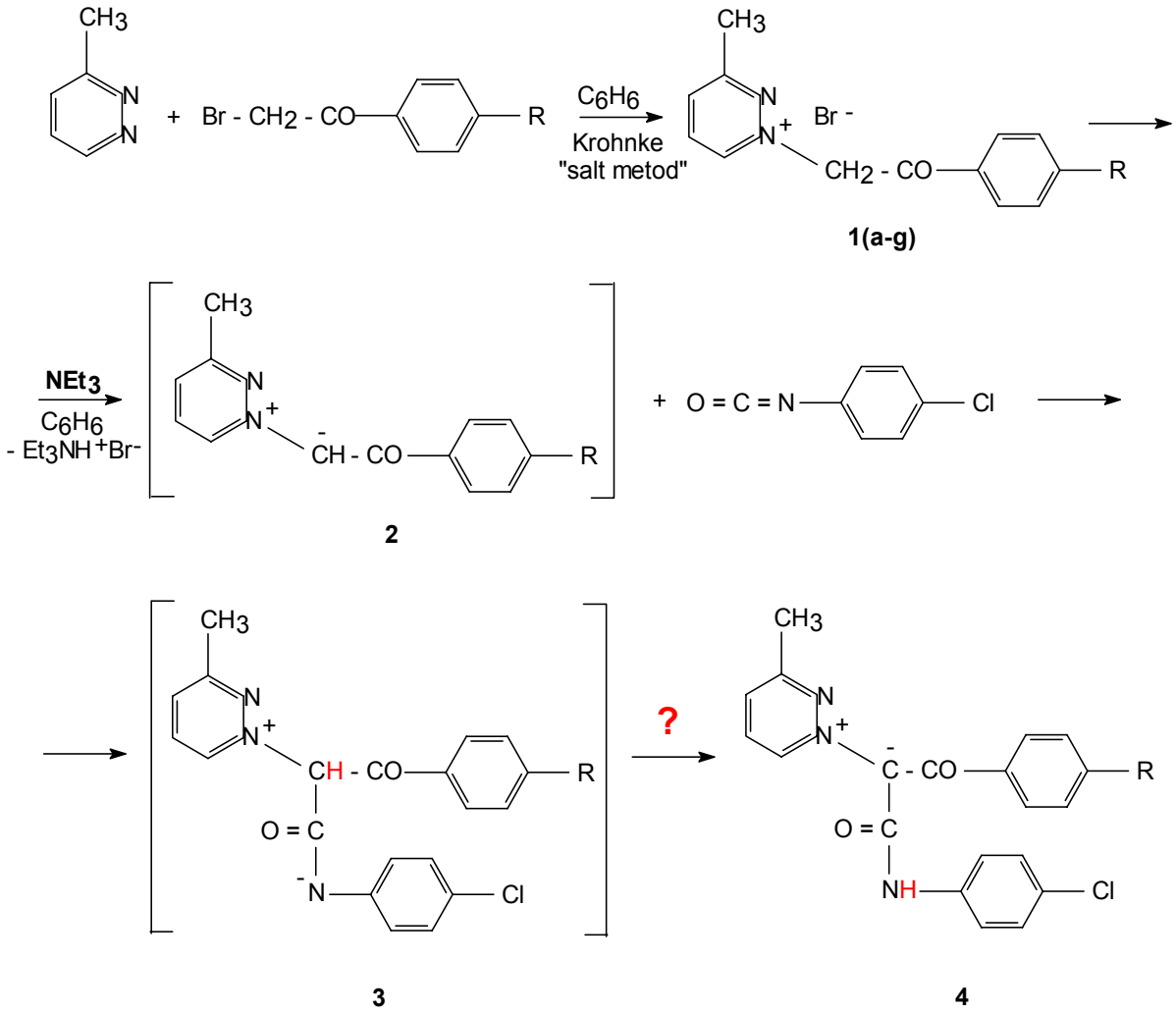
The experiments disclosed that the final product is different under different reaction conditions. We suppose that the reaction mechanism depends on the presence of triethylamine. Hence, when the most stable monoylide **2e** was separated with an aqueous solution of $K_2CO_3$ and treated with *p*-chlorophenyl isocyanate in benzene at room temperature, the reaction failed to produce any disubstituded ylide. In order to validate our hypothesis, we allowed several drops of triethylamine to react with the reaction mixture. Indeed, we got immediately the orange precipitate of substituted ylide **4e**. Moreover, the formation of **4e** final product in the absence of tertiary base was achieved only by raising the temperature at 60-70°C and only in a very low conversion, under 10% in yield.

Having reached an understanding over the factors that influence the prototropy we considered more deeply the reaction mechanism in connection with the reaction conditions.

### II. Theoretical Considerations

Following these experimental studies, a fundamental interest appeared for the understanding of the factors related to the presence of tertiary amine. Therefore, in parallel with the experimental work, we performed here a B3LYP theoretical investigation performed in the presence of a solvent on the possible mechanisms of prototropic rearrangement from **3** to **4**. We chose to limit our focus only to hydrogen substituted (**1a-4a)** compounds since this case seems most general and for reasons of computational cost. To the best of our knowledge, there are no computational studies in this field. Reaction pathways were explored on the transition states to discriminate some hypotheses and to propose the corresponding mechanisms for this part of the reaction sequence.

The first event in our study consisted in the addition of phenylisocyanate to monoylide **2** with **3** intermediate formations. The result of nucleophylic attack of ylide carbanion over isocyanate carbon consists in the simple bond formation and isocyanate C=N double bond cleavage, respectively. This reaction proceeds according Dewar statement of normally prohibited synchronous multibond processes, taking place in distinct steps, each involving the formation and/or breaking of only one bond.[13] As expected, the new formed C-C bond (2.17Å) in transition state **TS0** is significantly longer (1.58 Å) than the final bond length in the **3** intermediate, while C-N is found 1.247Å in **TS0** (Fig. 1).




| 1-4 | a | b | c | d | e | f | g |
|---|---|---|---|---|---|---|---|
| R | –H | –Br | –Cl | –F | $–NO_2$ | $–C_6H_5$ | $–OCH_3$ |

Scheme 1 – General reaction with unknown prototropic rearrangement final step.

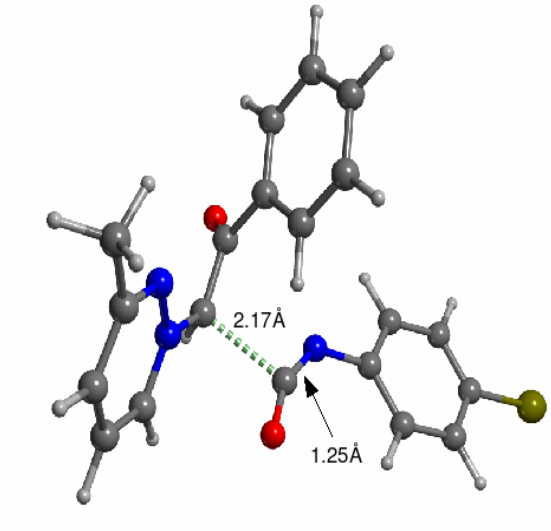



Fig. 1 – Geometry of **TS0**.

The computed barrier corresponds to the moderately endothermal reaction (Table 1). These findings are supported by the experimental normal condition for this reaction.

The final step of the general reaction (Scheme 1) consists in the prototropy from carbon to nitrogen in **3** intermediate that afforded disubstituted ylide **4**. Prototropic rearrangement could theoretically proceed by three plausible different pathways, as depicted in Figure 2. The first consist in the direct proton intramolecular migration from carbon to nitrogen (path a). Another reaction could represent the base-catalyzed prototropy *via* triethylamine used in monoylide releasing from its salt (path b). The third and the last one taken into account, the acid-catalyzed prototropic rearrangement by the small amounts of triethylamonium bromide remained in the reaction mixture (path c).

The energy profiles corresponding to the three pathways are distinguished in the Figure 3 by the same color code: blue for the absence of triethylamine (path a), green for triethylamine catalyze (path b), and red for the triethylamonium bromide catalyze (path c). The energy profile represents the relative energies related to the monoylide **2** and phenylisocyanate mixture considered as the initial state.

**(a) Internal proton migration**. For discussion, we will first suppose that intermediate **3** do not interact with triethylamine. In such circumstances the internal proton migration from ylide carbon to isocyanate nitrogen takes place through **TS1** transition state. The lengths of the breaking/forming bonds are given in Figure 4.

*Table 1*

Free energies (a.u.) and relative energies (kcal·mol$^{-1}$) corresponding to the equilibrium structures and transition states, and imaginary frequencies (cm$^{-1}$) of the transition states

| Structure | Free energies (a.u.) | Er (kcal·mol$^{-1}$) | Frequency (cm$^{-1}$) |
|---|---|---|---|
| **2+isocyanate** | -1546.025754 | 0 | |
| **TS0** | -1545.987056 | 24.3 | -282.6 |
| **3** | -1546.009395 | 10.3 | |
| **TS1** | -1545.968415 | 35.9 | -1744.2 |
| **4** | -1546.044581 | -11.8 | |
| **3+NEt$_3$** | -1838.170946 | - | |
| **TS2** | -1838.136447 | 21.6 | -1181.7 |
| **4+NEt$_3$** | -1838.206132 | -22.0 | |
| **3+Et$_3$NH$^+$Br$^-$** | -4410.34961 | - | |
| **I1** | -4410.392694 | -27.0 | |
| **TS3** | -4410.37239 | -14.3 | -1250.9 |
| **4+Et$_3$NH$^+$Br$^-$ Complex** | -4410.396916 | -29.7 | |

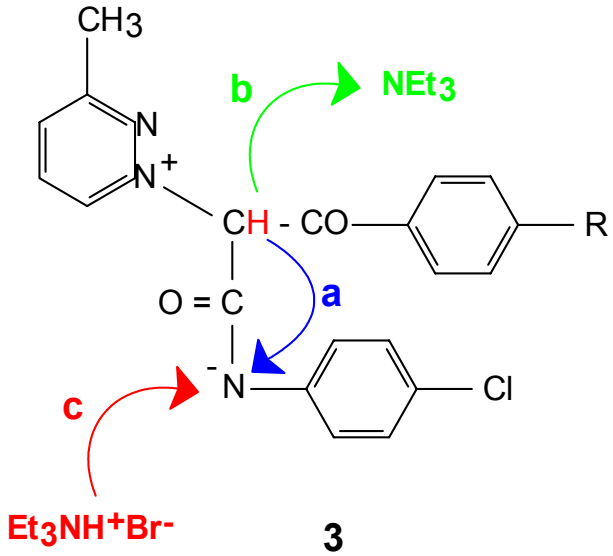



Fig. 2 – Plausible reaction pathways.

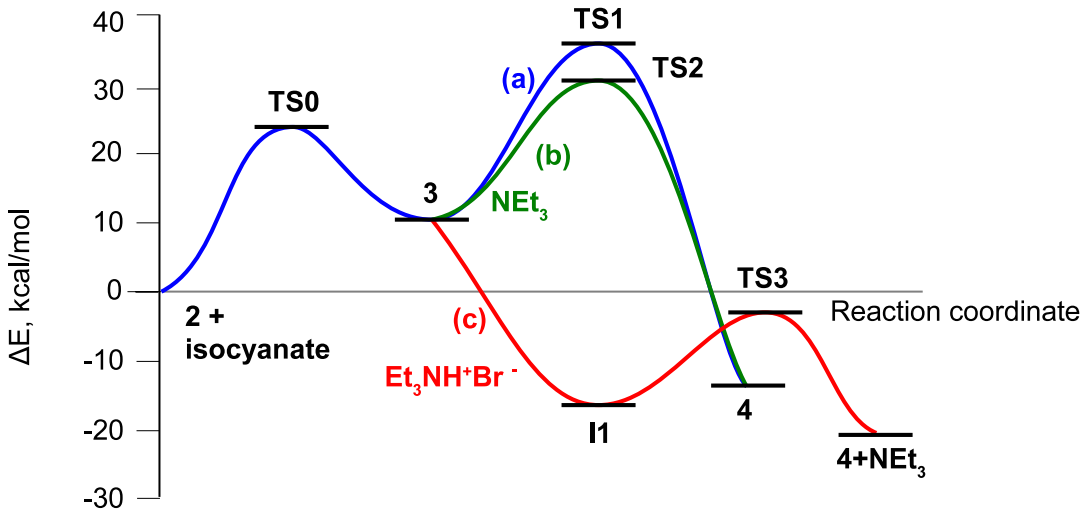



Fig. 3 – Relative energy profile related to the initial state.

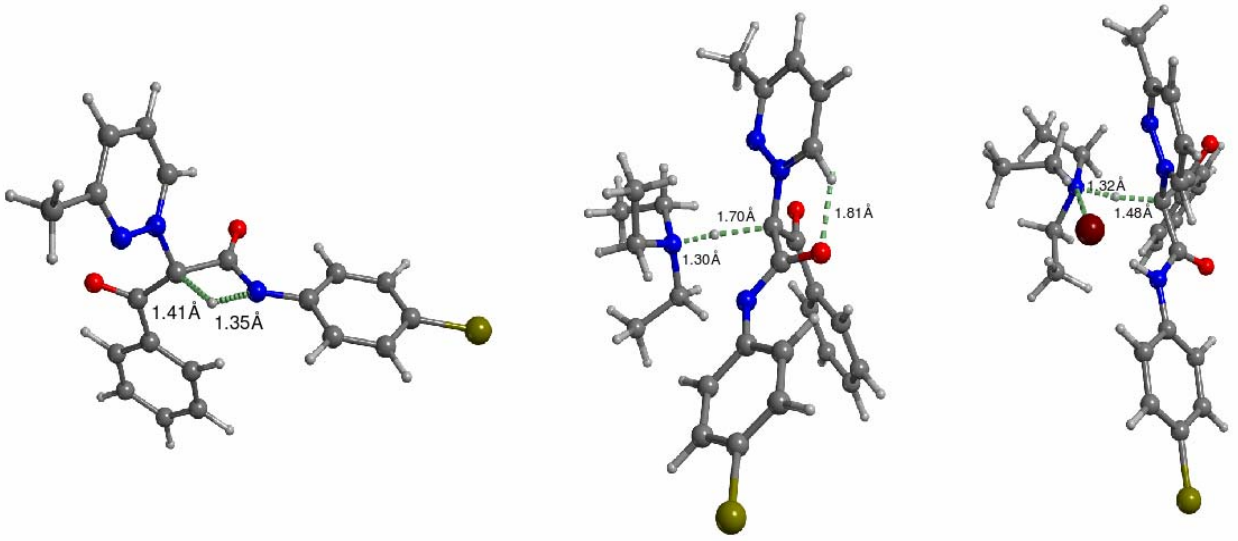



Fig. 4 – Geometries of **TS1**, **TS2** and **TS3**, respectively.

Energetically, one can remark the reaction in the absence of triethylamine is exothermic of 22.1 kcal $mol^{-1}$ but the barrier of 25.6 kcal $mol^{-1}$ is however high enough for a reaction easily occurring in mild condition (Tab. 1). Therefore this path was not considered probable.

As previous mentioned, experimentally attempts to afford **4e** final product starting from monoylide in the absence of tertiary base were successful but only raising the temperature at 60-70°C and in less than 10% yield.

**(b) Proton transfer by triethylamine**. The influence of triethylamine used to release ylide from its salt is the next path considered, since another mechanism is also possible. On this path one considered triethylamine attack over ylide hydrogen when the C-H bond is breaking and N-H bond is forming, through the **TS2** (Fig.3 and Fig. 4). The resulted triethylammonium ion transfers the proton to the isocyanate nitrogen without barrier and triethylamine is regenerated. No transition state corresponding to this last path was found.

Theoretical results are strongly supported by foregoing experimental study. Hence, the treatment of monoylide **2e**, previously separated with an aqueous solution of $K_2CO_3$, with p-chlorophenyl isocyanate in benzene at room temperature, afforded no transylidation. The addition of only several drops of triethylamine to the reaction mixture was sufficient to obtain the orange precipitate of disubstituted ylide **4e**.

**(c) Proton transfer via triethylamonium bromide**. We envisage here the reactivity of the small amounts of triethylamonium bromide existent in the reaction mixture. Triethylamonium bromide is provided by the reaction of triethylamine with either ylide salts **1** (Scheme 1) or intermediate **3** (path b). In this case, triethylamonium acid transfers the proton to the ylide nitrogen without transition state and barrier giving **I1** precomplex, the reaction being strongly exothermic (Fig. 3). This process is similar to the final interaction of path b. The resulted tertiary base extracts the proton from ylide carbon, into the next step, to afford the secondary ylide and regenerate the acid catalyst. The transition state for this reaction was found to be **TS3** that corresponds to a barrier of 12.7 kcal $mol^{-1}$. The geometry found for **TS2** and **TS3** are quite similar because both of them suppose proton transfer from ylide carbon to amine nitrogen. Moreover, in comparison with previous paths, the relative energies of **TS3** lie near the level of the final product. The acid catalyzed process was found to be strongly exothermic, having much greater value than activation energy, so that one can consider the process practically adiabatic (Fig. 3).

As a concluding remark over the global reaction (related to the nonreactive mixture of ylide **2** and phenylisocyanate), it is obvious that triethylamonium catalysis (path c) of -19.40 kcal $mol^{-1}$ is energetically considerably favored, compared to -11.80 kcal $mol^{-1}$ for the noncatalyzed (path a) or for base-catalyzed (path b) processes. It is the reason for one can predict that intermediate **3** even reacting kinetically with triethylamine on path (b) yet will finally prefer triethylamonium bromide once formed, and the reaction will follow path (c).

## COMPUTATIONAL METHODS

Geometry optimizations were performed for all equilibrium structures and transition states with DFT (B3LYP) method using the 6-31G basis set using Gaussian 98 program.[14] Geometry optimizations were performed without restrictions in order to locate extrema. The optimized geometries were verified to be equilibrium structures or transition states via frequency calculations. Free energies were calculated at 298 K and 1 atm and further considered as energetic criteria for the evolution of reaction. An equilibrium structure is characterized by all real frequencies while a transition state has one and only one imaginary frequency. In addition, for transition states intrinsic reaction coordinate (IRC) calculations were performed. An IRC calculation begins at a transition state and steps along the reaction path a fixed number of times in each direction toward the two minima that it connects.

The reactions take place experimentally in solution, using benzene as solvent and only gas phase calculations can be inadequate. The properties of molecules and transition states (TS) may differ between the gas phase and solution. The self-consistent reaction field (SCRF) methods model the solvent as a continuum of uniform dielectric constant ε which is the reaction field. According to the theory the solute is placed into a cavity within the solvent. A proper SCRF model for the calculation of stationary points on the energy hypersurface, minima as well as transition structures, is the Onsager reaction field model.[15] In this method, the solute occupies a fixed spherical cavity of radius $a_o$ within the solvent field; a dipole in the molecule will induce a dipole in the medium, and the electric field applied by the solvent dipole will in turn interact with the molecular dipole, leading to net stabilization.

## EXPERIMENTAL SECTION

**a. Materials and determinations.** All the reagents were obtained from commercial sources and were used as supplied. IR spectra were registered on a SPECORD 71 spectrophotometer in KBr; $\nu_{max}$ ($cm^{-1}$) is given for the main absorption bands. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker Avance instrument (400 MHz) using TMS (δH 0.0 ppm) as internal reference. MS spectra were recorded on a Bruker spectrometer. Melting points were determined on a MELTEMP II apparatus and are uncorrected.

**b. General procedure for salts 1(a–g) preparation**
Different 4-substituted bromoacetophenone (1 mmol) was dissolved in benzene (10 mL) and then 3-methylpyridazine (1 mmol) in benzene (10 mL,) was added dropwise. The resulting mixture was stirred for 24 h at room temperature. The resulting mixture was filtered under vacuum and the crude products were purified by recrystallization from methanol.
*N-phenacyl-3-methyl-pyridazinium bromide* **(1a)** Obtained according to the general procedure for salts from 0.2 g bromoacetophenone and 0.1 mL 3-methylpyridazine; cream-colored. Yield 81 %. M.p. 194-195 ºC. IR (KBr, ν, $cm^{-1}$): 1705 (C=O); 1605, 1485, 1470, 1420 (C=C, C=N); 2980 (C-H aliph). $^1H$ NMR (TMS, DMSO, δ ppm): 9.00-8.70 (m, 2H), 10.00-9.85 (d, 1H, $J$ = 6.0 Hz), 6.70 (s, 2H), 8.25-8.10 (d, 2H, $J$ = 9 Hz), 7.90-7.55 (m, 3H), 2.80 (s, 3H: $CH_3$). Anal. Calcd. For $C_{13}H_{13}BrN_2O$: C, 53.26; H, 4.47; N, 9.57. Found: C, 53.00; H, 4.14; N, 9.16 %.

*N-(p-bromo-phenacyl)-3-methyl-pyridazinium bromide* **(1b)** Obtained according to the general procedure for salts from 0.278 g ω-bromo-4-bromo-acetophenone and 0.1 mL 3-methylpyridazine; cream-colored compound. Yield 87 %. M.p. 201-202 ºC. IR (KBr, ν, $cm^{-1}$): 1705 (C=O); 1600, 1485, 1470, 1410 (C=C, C=N); 3100 (C-H aliph.). $^1$H NMR (TMS, DMSO, δ ppm): 8.95-8.70 (m, 2H), 10.00-9.85 (d, 1H, *J* = 6.0 Hz), 6.75 (s, 2H), 8.20-8.00 (d, 2H, *J* = 9 Hz), 7.90-7.65 (d, 2H, *J* = 9 Hz), 2.80 (s, 3H: $CH_3$). Anal. Calcd. For $C_{13}H_{12}Br_2N_2O$: C, 41.93; H, 3.22; N, 7.53. Found: C, 42.10; H, 3.07; N, 7.98 %.

*N-(p-chloro-phenacyl)-3-methyl-pyridazinium bromide* **(1c)** Obtained according to the general procedure for salts from 0.278 g ω-bromo-4-chloro-acetophenone and 0.1 mL 3-methylpyridazine; beige-rosy colored compound. Yield 91.5 %. M.p. 218-219 ºC. IR (KBr, ν, $cm^{-1}$): 1710 (C=O); 1600, 1485, 1470, 1410 (C=C, C=N); 3100 (C-H aliph.). $^1$H NMR (TMS, DMSO, δ ppm): 8.83-8.65 (m, 2H), 9.92-9.90 (d, 1H, *J* = 6.0 Hz), 6.81 (s, 2H), 8.18-8.11 (d, 2H, *J* = 9 Hz), 7.76-7.73 (d, 2H, *J* = 9 Hz), 2.81 (s, 3H: $CH_3$). $^{13}$C NMR (DMSO-$d_6$, δ ppm): 189.64, 153.97, 151.16, 139.91, 135.38, 134.40, 132.74, 128.63, 127.93, 70.0, 21.52. MS: *m*/*z* (relative intensity) 246 ($M^+$-Br, PB), 140 (95), 108 (60). Anal. Calcd. For $C_{13}H_{12}BrClN_2O$: C, 47.63; H, 3.66; N, 8.55. Found: C, 47.94; H, 3.42; N, 8.31 %.

*N-(p-fluoro-phenacyl)-3-methyl-pyridazinium bromide* **(1d)** Obtained according to the general procedure for salts from 0.2 g ω-bromo-4-fluoro-acetophenone and 0.1 mL 3-methylpyridazine; beige-rosy colored compound. Yield 96.46 %. M.p. 208 ºC. IR (KBr, ν, $cm^{-1}$): 1710 (C=O); 1600, 1485, 1470, 1410 (C=C, C=N); 3100 (C-H aliph.). $^1$H NMR (TMS, DMSO, δ ppm): 8.79-8.76 (dd, 1H), 8.67-8.65 (d, 1H), 9.80-9.78 (d, 1H, *J* = 6 Hz) 6.74 (s, 2H), 8.21-8.18 (d, 2H, *J* = 9 Hz), 7.54-7.50 (d, 2H, *J* = 9 Hz), 2.82 (s, 3H: $CH_3$). $^{13}$C NMR (DMSO-$d_6$, δ ppm): 189.64, 165.30, 165.20, 150.20, 138.88, 135.49, 132.25, 132.14, 130.67, 70.49, 21.06. MS: *m*/*z* (relative intensity) 231 ($M^+$-Br, PB), 124 (95), 107 (60). Anal. Calcd. For $C_{13}H_{12}BrFN_2O$: C, 48.90; H, 3.76; N, 8.78. Found: C, 48.41; H, 3.27; N, 8.60 %.

*N-(p-nitro-phenacyl)-3-methyl-pyridazinium bromide* **(1e)** Obtained according to the general procedure for salts from 0.24 g ω-bromo-4-nitro-acetophenone and 0.1 mL 3-methylpyridazine; cream-colored compound. Yield 80 %. M.p. 205-207 ºC. IR (KBr, ν, $cm^{-1}$): 1705 (C=O); 1615, 1550, 1485, 1430 (C=C, C=N); 1530, 1355 ($NO_2$); 2980 (C-H aliph.). $^1$H NMR (TMS, DMSO, δ ppm): 8.95-8.75 (m, 2H), 10.00-9.85 (d, 1H, *J* = 6.5 Hz) 6.90 (s, 2H), 8.60-8.20 (d, 2H, *J* = 9 Hz), 2.80 (s, 3H: $CH_3$). Anal. Calcd. For $C_{13}H_{12}BrN_3O_3$: C, 46.15; H, 3.55; N, 12.42. Found: C, 46.10; H, 3.70; N, 11.76 %.

*N-(p-phenyl-phenacyl)-3-methyl-pyridazinium bromide* **(1f)** Obtained according to the general procedure for salts from 0.275 g ω-bromo-4-phenyl-acetophenone and 0.1 mL 3-methylpyridazine; white-colored compound. Yield 81 %. M.p. 209-210 ºC. IR (KBr, ν, $cm^{-1}$): 1705 (C=O); 1610, 1580, 1480, 1440 (C=C, C=N); 2980 (C-H aliph.); 3100-3000 (C-H arom.). $^1$H NMR (TMS, DMSO, δ ppm): 9.00-8.70 (m, 2H), 10.00-9.85 (d, 1H, *J* = 6 Hz), 6.70 (s, 2H), 8.25-8.10 (d, 2H, *J* = 9 Hz), 7.90-7.55 (m, 7H), 2.80 (s, 3H: $CH_3$). Anal. Calcd. For $C_{19}H_{17}BrN_2O$: C, 61.79; H, 4.60; N, 7.59. Found: C, 61.43; H, 4.37; N, 7.95 %.

*N-(p-methoxy-phenacyl)-3-methyl-pyridazinium bromide* **(1g)** Obtained according to the general procedure for salts from 0.23 g ω-bromo-4-methoxy-acetophenone and 0.1 mL 3-methylpyridazine; white-colored compound. Yield 93 %. M.p. 203-205 ºC. IR (KBr, ν, $cm^{-1}$): 1695 (C=O); 1610, 1585, 1510, 1435, 1430 (C=C, C=N); 1260, 1040 (C-O-C); 2980 (C-H aliph.). $^1$H NMR (TMS, DMSO, δ ppm): 8.90-8.55 (m, 2H), 9.95-9.80 (d, 1H, *J* = 6.5 Hz), 6.65 (s, 2H), 8.15-7.90 (d, 2H, *J* = 9 Hz), 7.20-7.00 (d, 2H, *J* = 9 Hz), 3.90 (s, 3H: $OCH_3$), 2.80 (s, 3H: $CH_3$). Anal. Calcd. For $C_{14}H_{15}BrN_2O_2$: C, 52.01; H, 4.64; N, 8.67. Found: C, 52.36; H, 4.14; N, 8.18 %.

**c. General procedure for transylidation with phenylisocyanate**

To a stirred suspension of **1 (a-g)** cycloimmonium salt (2 mmol) in benzene (30 mL) heated on a steam bath at 50ºC triethylamine (4 mmol) was added dropwise during 30 min in order to release the ylides **2 (a-g)**. The bromhidrate precipitate was separated and to the cooled filtrate a solution of phenylisocyanate (2 mmol) in benzene was added under stirring. The orange precipitate of disubstituted ylide appeared immediately. The reaction mixture was kept under magnetic stirring for 2-3 h at room temperature to reach completion. The final product **4** (**a-g**) was filtrated and recrystallized from methanol as orange crystals.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(benzoyl)-methylide* **(4a)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 82 %. M.p. 156-157 ºC. IR (KBr, ν, $cm^{-1}$): 1655 (C=O amide); 1510 (C=O cetone); 1550, 1290 (C-N amide); 1600, 1450 (C=C, C=N); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.29 (d, 1H, *J* = 7.5 Hz), 8.28 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 7.00-7.54 (m, 9H), 2.40 (s, 3H: $CH_3$). Anal. Calcd. For $C_{20}H_{16}ClN_3O_2$: N, 11.49. Found: N, 11.76 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-bromo-benzoyl)-methylide* **(4b)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 82 %. M.p. 159-162 ºC. IR (KBr, ν, $cm^{-1}$): 1650 (C=O amide); 1500 (C=O cetone); 1550, 1290 (C-N amide); 1600, 1450 (C=C, C=N); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.80-9.60 (d, 1H, *J* = 7.5 Hz), 8.55-8.30 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 8.25-8.05 (d, 1H, *J* = 8 Hz), 7.80-7.00 (m, 8H), 2.60 (s, 3H: $CH_3$). Anal. Calcd. For $C_{20}H_{15}BrClN_3O_2$: N, 9.45. Found: N, 9.90 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-chloro-benzoyl)-methylide* **(4c)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 80 %. M.p. 167-169 ºC. IR (KBr, ν, $cm^{-1}$): 1650 (C=O amide); 1500 (C=O cetone); 1550, 1290 (C-N amide); 1600, 1450 (C=C, C=N); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.80-9.60 (d, 1H, *J* = 7.5 Hz), 8.55-8.30 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 8.25-8.05 (d, 1H, *J* = 8 Hz), 7.80-7.00 (m, 8H), 2.60 (s, 3H: $CH_3$). Anal. Calcd. For $C_{20}H_{15}Cl_2N_3O_2$: N, 10.50. Found: N, 10.90 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-fluoro-benzoyl)-methylide* **(4d)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 76 %. M.p. 165-168 ºC. IR (KBr, ν, $cm^{-1}$): 1650 (C=O amide); 1500 (C=O cetone); 1550, 1290 (C-N amide); 1600, 1450 (C=C, C=N); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.80-9.60 (d, 1H, *J* = 7.5 Hz), 8.55-8.30 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 8.25-8.05 (d, 1H, *J* = 8 Hz), 7.80-7.00 (m, 8H), 2.60 (s, 3H: $CH_3$). Anal. Calcd. For $C_{20}H_{15}ClFN_3O_2$: N, 10.95. Found: N, 10.90 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-nitro-benzoyl)-methylide* **(4e)** The preparation was carried out as described above for the transylidation with phenylisocyanate; dark-orange crystals. Yield 89 %. M.p. 187-188 ºC. IR (KBr, ν, $cm^{-1}$): 1640 (C=O amide); 1490 (C=O cetone); 1555, 1290 (C-N amide); 1600, 1470, 1405, 1380 (C=C, C=N); 1520, 1345 ($NO_2$); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.55 (s, 1H: NH), 9.85-9.60 (d, 1H, *J* = 7.5 Hz), 8.50-8.25 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 8.20-8.05 (d, 1H, *J* = 8 Hz), 7.65-7.05 (m, 8H), 2.65 (s, 3H: $CH_3$). Anal. Calcd. For $C_{20}H_{15}ClN_4O_4$: N, 13.64. Found: N, 13.01 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-phenyl-benzoyl)-methylide* **(4f)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 70.2 %. M.p. 164-165 ºC. IR (KBr, ν, $cm^{-1}$): 1645 (C=O amide); 1550, 1290 (C-N amide); 1600, 1470, 1405, 1380 (C=C, C=N); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.30 (d, 1H, *J* = 7.5 Hz), 8.29 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 7.85 (d, 1H, *J* = 8 Hz), 7.47-6.95 (m, 13H), 2.40 (s, 3H: $CH_3$). Anal. Calcd. For $C_{26}H_{20}ClN_3O_2$: N, 9.51. Found: N, 9.01 %.

*3-methyl-pyridazinium-1-(4''-chloroanilido)-1-(4'-methoxy-benzoyl)-methylide* **(4g)** The preparation was carried out as described above for the transylidation with phenylisocyanate. Yield 59 %. M.p. 172-173 ºC. IR (KBr, ν, $cm^{-1}$): 1650 (C=O amide); 1510 (C=O cetone); 1550, 1290 (C-N amide); 1600, 1450 (C=C, C=N); 1260 (O-$CH_3$); 3100-3000 (C-H arom.); 3300 (N-H amide). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 12.50 (s, 1H: NH), 9.16 (d, 1H, *J* = 7.5 Hz), 8.28 (t, 1H, *J* = 7.5 Hz, *J* = 8 Hz), 7.82 (d, 1H, *J* = 8 Hz), 7.46-6.93 (m, 13H), 3.30 (s, 3H: O-$CH_3$), 2.40 (s, 3H: $CH_3$).

**d. General procedure for monoylides 2(a–g) preparation**

In order to estimate the influence of triethylamine, monoylides were separated. Hence, to a solution of the corresponding salts **1 (a-g)** (0.2 g) in water (20 mL) an aquous solution of $K_2CO_3$ 40% was added dropwise under stirring until the pH = 8-9. Monoylides precipitated rapidly and were removed by filtration, dried and recryastallized from the appropriate solvents. **Monoylide 2e** Obtained as presented in general procedure for monoylide preparation; was found as radish crystals. M.p. 145-146 ºC. IR (KBr, ν, $cm^{-1}$): 1550 (C=O est.); 1590, 1475, 1445 (C=C, C=N); 3100-3000 (C-H aliph.). $^1$H NMR (TMS, $CDCl_3$, δ ppm): 8.00-7.25 (m, 2H, *J* = 11.5 Hz), 8.00-7.25 (m, 1H, *J* = 11.5 Hz, *J* = 6.5 Hz), 11.00-10.80 (d, 1H, *J* = 6.5 Hz), 8.00-7.25 (m, 5H), 2.55 (s, 3H: $CH_3$). Anal. Calcd. For $C_{13}H_{11}N_3O_3$: C, 60.70; H, 4.61; N, 16.33. Found: C, 60.21; H, 4.37; N, 15.90 %.

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