

4-Methylpyrimidinium Ylides, 1

Geanina Mangalagiu,^[a] Ionel Mangalagiu,^{*[a]} Ionel Humelnicu,^[a] and Magda Petrovanu^[a]**Keywords:** 4-Methylpyrimidine / Ylides / Quantum chemical calculations

For the first time in the pyrimidinium ylides series we present a theoretical and experimental study concerning the structure, stability and reactivity of pyrimidinium ylides and interesting correlations between these properties. 4-Methylpyrimidinium ylides are relatively stable compounds, their stability varying with the nature of the ylide carbanion substituent. The more electron-withdrawing these substituents, the more the anionic charge is delocalized and

therefore the higher the stability. The data from experiments and quantum chemical calculations are in agreement with each other. The quantum chemical calculations show the possibility of using pyrimidinium ylides as nucleophilic reagents as well as 1,3-dipoles in reaction with appropriate reagents. Eight new pyrimidine compounds (4 salts and 4 ylides) were obtained.

Introduction

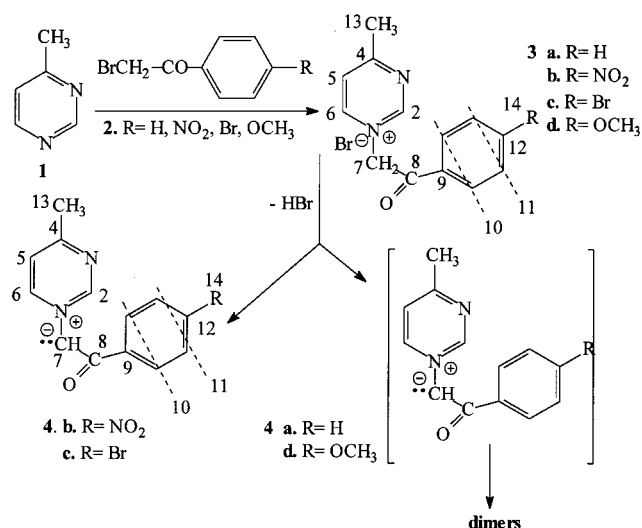
In previous work,^[1–4] the synthesis, structure and reactivity of 1,2-diazinium ylides derived from pyridazine and phthalazine (unsubstituted or substituted) have been studied. The main target in this previous work was the synthesis of new stable 1,2-diazine ylides, and the correlation between their structure, stability and reactivity (biological, acid-base, semiconductor properties, etc.). Continuing in this line of research, it was decided to study the 1,3-diazine ylides derived from 4-methylpyrimidine, with the intention of increasing both the breadth and depth of knowledge in the field of diazine ylides.

Results and Discussion.

In order to obtain new pyrimidinium ylides derived from 4-methylpyrimidine the salt method of Kröhnke was used.^[5] Thus, *N*-(*p*-*R*-benzoyl)pyrimidinium salts **3a–d** were prepared by treating 4-methylpyrimidine (**1**) with *p*-*R*-phenacyl bromides **2**, which, in an aqueous solution of alkaline carbonates, afforded the corresponding pyrimidinium ylides **4a–d** (Scheme 1).

In order to establish the correlation between structure, stability and reactivity in the 4-methylpyrimidinium ylides a series of theoretical calculations were carried out using the General Theory of Perturbation Limited to the Frontier Molecular Orbitals.^[6–11] The geometry of the 4-methylpyrimidinium ylides (Figure 1), the atomic charges, the coefficients of the atomic orbitals, and the values of the energy of the frontier molecular orbitals were calculated using the AM1 method (Table 1).^[12]

The data from Figure 1 show the following:



Scheme 1. Reaction pathway to obtain 4-methylpyrimidinium ylides

- The ylide carbanion center C^7 , the ylide nitrogen atom N^1 and the α -endocyclic carbon atoms are co-planar (valence angles to the atoms involved ca. 120° , torsion angles 0° or 180°).
- The bond lengths ylide carbanion center (C^7)–ylide nitrogen atom (N^1), N^1 – C^2 , and N^1 – C^6 are ca. $1.40 \text{ \AA}$ (intermediate between simple and double bond).

The analysis of the data from Table 1 leads to the following conclusions:

- The ylide carbanion centers C^7 have a negative atomic charge, subunity, but significant (larger than all the other charges on the molecule).
- The ylide nitrogen atoms N^1 have a positive atomic charge, subunity, significant but smaller (in absolute value) than for the ylide carbanion centers.
- The α -endocyclic carbanion centers C^2 and C^6 have small negative atomic charges, both being subunity.

The fact that the total atomic charges are subunity indicates the delocalization of the anionic charge from the ylide

^[a] “Al. I. Cuza” University Iasi,
B-dul Copou, No. 11, RO-6600 Iasi, Romania
Fax: (internat.) + 40-32/213330
E-mail: ionelm@uaic.ro

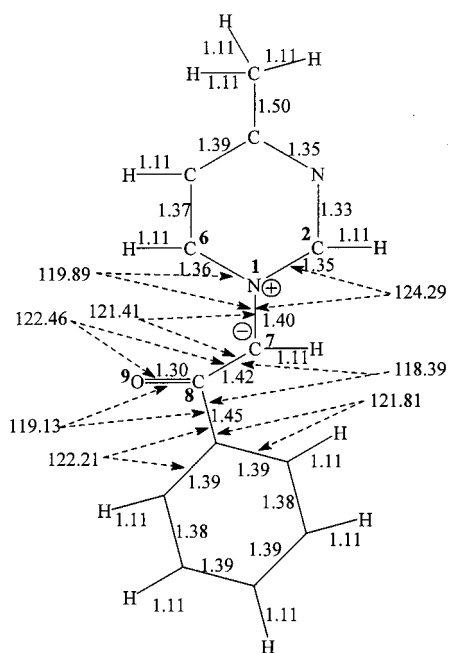


Table 2. ^1H -NMR data (δ values, J [Hz]) and carbonyl valence group vibration data [cm^{-1}] of pyrimidinium salts **3**

Salts	2-H	5-H	6-H	7-H	10-H	11-H	13-H	14-H	$\nu_{\text{C=O}}$
3a	9.70 s	8.50–8.45 d, $J = 5.5$	9.45–9.38 d, $J = 5.5$	8.30–8.20 2 H, d, $J = 9.0$	—	7.90–7.50 2 H, m, $J = 9.0$	2.90 s (CH_3)	7.90–7.50 m	1695 —
3b	9.64 s	8.50–8.45 d, $J = 5.4$	9.22–9.18 d, $J = 5.4$	6.50 s	8.32–8.22 2 H, d, $J = 9.0$	8.38–8.32 2 H, d, $J = 9.0$	2.85 s (CH_3)	—	1710 —
3c	9.60 s	8.30–8.25 d, $J = 5.6$	9.16–9.11 d, $J = 5.6$	6.45 s	7.85–7.70 m, 2 H	7.85–7.70 m, 2 H	2.80 s (CH_3)	—	1698 —
3d	9.60 s	8.26–8.20 d, $J = 5.6$	9.20–9.15 d, $J = 5.6$	6.40 s	8.05–7.95 2 H, d, $J = 9.4$	7.20–7.14 2 H, d, $J = 9.4$	2.80 s (CH_3)	3.80 s (OCH_3)	1710 —

dergo a rapid dimerisation process immediately after preparation, to afford an ylide/dimer mixture (Scheme 1). This means that, when the substituent R has an electron-withdrawing effect (as in the case of a nitro group) the delocalization of ylide carbanion charge to the benzoyl group is favoured and consequently the stability of the ylides is higher (Figure 3). When the substituent R has a repulsive effect (as in the case of a methoxy group) the delocalization of the ylide carbanion charge to the benzoyl group is unfavoured, consequently the stability of the ylides decreases and the dimerisation process occurs easily (Figures 1 and 3). The structure of the new pyrimidine compounds was confirmed by elemental and spectral (IR, ^1H and ^{13}C NMR) analyses. Elemental (C, H, N) analyses are compatible with the proposed structures for the salts and ylides. Essential data are furnished by spectral analysis. In the IR spectra of salts **3** (Table 2) the signals corresponding to the ketone group are situated between 1710 (R = NO_2 , **3b**) and 1680 cm^{-1} (R = OCH_3 , **3d**), in accordance with the effect of the substituent in *para* position of the phenyl ring.

In the ^1H -NMR spectra (Table 2) the most important signals are those of 2-H, 6-H and 7-H. As can be seen in Table 2 the 2-H signal appears at $\delta \approx 9.60$ (s), the 6-H signal at $\delta \approx 9.45$ – 9.10 (d, $J \approx 5.5$ Hz) and the 7-H signal at $\delta \approx 6.60$ – 6.40 (s), in accordance with the proposed structure. The ^{13}C -NMR spectrum of **3b** also confirms the structure: C-8: $\delta = 189.66$ (alkyl aryl ketone); C-2: $\delta = 177.72$ [pyrimidine carbon atom (one α -nitrogen, one positive α -nitrogen atom)]; C-6: $\delta = 172.28$ [pyrimidine carbon atom (one positive α -nitrogen, one α -carbon atom)]; C-7: $\delta = 63.42$ [alkyl carbon atom (α -ketone, positive α -nitrogen from pyrimidine)]. All the remaining signals from IR and NMR spectra are in accordance with the proposed structure for the pyrimidine salts. The IR spectra of ylides **4** confirm the proposed structure. Thus, the signal for the ketone group appears at 1660 and 1670 cm^{-1} , for ylides **4b** and **4c** respectively. The difference $\tilde{\nu}_{\text{C=O(salts)}} - \tilde{\nu}_{\text{C=O(ylides)}} \approx 50\text{ cm}^{-1}$ is in accordance with the delocalization phenomena of the negative charge from the ylide carbanion to the phenyl ring (Figures 3 and 4) and confirms our previous supposition. The ^1H -NMR spectrum of ylide **4b** also confirms the structure. There are two signals: $\delta = 8.40$ – 7.50 [m, 8 H (7 aromatic and 1 ylidic proton)]; $\delta = 2.65$ [s, 3 H (methyl)]. The IR spectra and melting points of ylides **4a** and **4d** show that we have a mixture of the ylide and, prob-

ably, the dimer [two ketone bands: $\tilde{\nu} = 1675\text{ cm}^{-1}$ (ylide) 1705 (dimer); large range of melting points].

Conclusions

1. The stability of 4-methylpyrimidinium ylides varies with the nature of the ylide carbanion substituent. The higher the electron-withdrawing effect of these substituents, the more is the anionic charge delocalized and therefore the higher the stability. The experimental data and quantum chemical calculations confirm this hypothesis and are in agreement with each other.

2. The quantum chemical calculations show the possibility of using pyrimidinium ylides as nucleophilic reagents as well as 1,3-dipoles in reactions with appropriate reagents.

3. Eight new pyrimidine compounds, 4 salts and 4 ylides, have been obtained. The dimer structures and properties remain to be studied.

Experimental Section

^1H and ^{13}C NMR: Gemini 200 MHz spectrometer, internal standard, $[\text{D}_6]\text{DMSO}$, coupling constants are given in Hz. – IR: SPECORD-71 spectrometer (KBr). – M.p.: Uncorrected values. – Quantum chemical calculations: HYPERCHEM 5.02 program.^[13]

General Procedure A to Obtain Pyrimidinium Salts: 4-Methylpyrimidine (0.2 mL, 2 mmol) and ω -bromo-*p*-acetophenone (2 mmol) were dissolved in acetone (10 mL). The solution was heated to reflux with a steam bath for 1 h. Ethyl ether was then added and the pyrimidinium salt obtained was filtered rapidly and dried in vacuo.

General Procedure B to Obtain Pyrimidinium Ylides: The 4-methylpyrimidinium salt (1 mmol) was dissolved in water (50 mL) and treated with a 40% aqueous solution of K_2CO_3 . The ylide was filtered, washed with a large amount of water and dried in vacuo.

***N*-Benzoyl-4-methylpyrimidinium Bromide (3a):** Prepared according to General Procedure A using 0.398 g of ω -bromoacetophenone. Cream-yellow crystals. Yield 0.562 g (96%), m.p. 163 – 165°C . – IR (KBr): $\tilde{\nu} = 3100$ – 3050 cm^{-1} ($=\text{C-H}$), 2980 ($-\text{C-H}$), 1695 (C=O), 1620 , 1550 , 1455 (C=C , C=N). – ^1H NMR: Table 2. – $\text{C}_{13}\text{H}_{13}\text{BrN}_2\text{O}$ (293): calcd. C 53.26, H 4.47, N 9.56; found C 53.10, H 4.45, N 9.30.

4-Methyl-*N*-(*p*-nitrobenzoyl)pyrimidinium Bromide (3b): Prepared according to General Procedure A using 0.488 g of ω -bromo-*p*-nitroacetophenone. Yellow crystals. Yield 0.622 g (92%), m.p. 165 – 167°C . – IR (KBr): $\tilde{\nu} = 3100$ – 3050 cm^{-1} ($=\text{C-H}$), 1710

(C=O), 1635, 1600, 1450, 1400 (C=C, C=N), 1515, 1355 (NO₂). – ¹H NMR: Table 2. – ¹³C NMR ([D₆]DMSO): δ = 189.6 (C-8, C=O), 177.7 (C-2), 172.2 (C-6), 153.7 (C-12), 151.9 (C-4), 150.5 (C-9), 128.2 (C-10), 124.1 (C-11), 122.8 (C-5), 63.4 (C-7, CH₂), 25.4 (C-13, CH₃). – C₁₃H₁₂BrN₃O₃ (338): calcd. C 46.17, H 3.58, N 12.43; found C 46.10, H 3.65, N 12.40.

N-(p-Bromobenzoyl)-4-methylpyrimidinium Bromide (3c): Prepared according to General Procedure A using 0.556 g of p,ω-dibromoacetophenone. Yellow crystals. Yield 0.714 g (96%), m.p. 166–167°C. – IR (KBr): $\tilde{\nu}$ = 3100–3050 cm⁻¹ (=C–H), 2980 (–C–H), 1698 (C=O), 1625, 1575, 1460 (C=C, C=N). – ¹H NMR: Table 2. – C₁₃H₁₂Br₂N₂O (372): calcd. C 41.97, H 3.25, N 7.53; found C 41.80, H 3.30, N 7.30.

N-(p-Methoxybenzoyl)-4-methylpyrimidinium Bromide (3d): Prepared according to General Procedure A using 0.458 g of ω-bromo-p-methoxyacetophenone. Cream-colored crystals. Yield 0.581 g (90%), m.p. 138–141°C. – IR (KBr): $\tilde{\nu}$ = 3100–3050 cm⁻¹ (=C–H), 2980 (–C–H), 1680 (C=O), 1630, 1605, 1455 (C=C, C=N), 1260, 1030 (C–O–C). – ¹H NMR: Table 2. – C₁₄H₁₆BrN₂O₂ (323): calcd. N 8.67; found N 8.35.

4-Methylpyrimidinium p-Nitrobenzoylmethylide (4b): Prepared according to General Procedure B using compound **3b** (0.338 g, 1.0 mmol). Cherry-colored compound. Yield 0.254 g (99%), m.p. 153–156°C. – IR (KBr): $\tilde{\nu}$ = 3050 cm⁻¹ (=C–H), 2980 (–C–H), 1660 (C=O), 1570, 1465, 1410 (C=C, C=N), 1510, 1355 (NO₂). – C₁₃H₁₁N₃O₃ (257): calcd. N 16.33; found N 16.20.

4-Methylpyrimidinium p-Bromobenzoylmethylide (4c): Prepared according to General Procedure B using compound **3c** (0.372 g, 1.0 mmol). Red compound. Yield 0.288 g (99%), m.p. 138–140°C. – IR (KBr): $\tilde{\nu}$ = 3050 cm⁻¹ (=C–H), 2980 (–C–H), 1670 (C=O), 1590, 1490, 1455, 1400 (C=C, C=N). – C₁₃H₁₁BrN₂O (291): calcd. N 9.62; found N 9.45.

4-Methylpyrimidinium Benzoylmethylide (4a): CAUTION: Hazardous compound! Prepared according to General Procedure B using compound **3a** (0.293 g, 1.0 mmol). Mixed with dimer, orange/brownish. Yield 0.210 g (99%), m.p. 125–130°C. – IR (KBr): $\tilde{\nu}$ = 3050 cm⁻¹ (=C–H), 2980 (–C–H), 1705 (C=O from dimer), 1675 (C=O from ylide), 1605, 1590, 1465, 1400 (C=C, C=N).

4-Methylpyrimidinium p-Methoxybenzoylmethylide (4d): CAUTION: Hazardous compound! Prepared according to General Procedure B using compound **3d** (0.323 g, 1.0 mmol). Mixed with dimer, orange. Yield 0.240 g (99%), m.p. 140–145°C. – IR (KBr): $\tilde{\nu}$ = 3050 cm⁻¹ (=C–H), 2980 (–C–H), 1680 (C=O from dimer), 1670 (C=O from ylide), 1600, 1515, 1465, 1420, 1400 (C=C, C=N), 1265, 1035 (C–O–C).

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