Diazinium carbalkoxy methylides

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Dedicated to C. D. Nenitescu (Bucharest) on the occasion of the 100th anniversary
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Abstract
In this paper we present study concerning the structure, the stability and the reactivity of some new diazinium ylides. Pyrimidinium- and pyridazinium carbalkoxy methylides prove to be stable compounds with the exception of 3-(p-chlorophenyl)pyridazinium carbethoxymethylide 12 which traps atmospheric CO₂ leading to a ylide-betaine. A selective way to increase the yield of ylide or betaine has been found. An interesting correlation between structure, stability and reactivity has been found. The structure of ylides and betaine has been proven through elemental and spectral (IR, NMR, MS) analysis as well as by chemical methods. Thus, the ability of diazinium carbalkoxy methylides to react with symmetrical substituted activated alkynes (DMAD) has been studied. Nine new compounds derived from diazines have been obtained.

Keywords: Cycloimmonium ylides, diazine, pyridazine, pyrimidine, betaine, structure, stability, reactivity, cycloaddition, DMAD, azabicyclic compounds

Introduction
As we show in some recent papers,¹²,³ the chemistry of cycloimmonium ylides has been widely discussed.⁴-⁷ In previous research work we presented a detailed study concerning the syntheses, structure, stability and reactivity of some new 3-p-halophenylpyridazine salts and ylides⁸,⁹ and 4-methylpyrimidine salts and ylides.¹⁰ In these ylides the substituent of the ylide carbanion was a p-R-benzoyl radical with a medium electron-withdrawing effect. Continuing our research in this field we decide to change the substituents of the ylide carbanion with carbalkoxy (carbemthoxy or carbethoxy) groups and, consequently, to see the influence concerning the synthesis, structure, stability, reactivity and properties in the diazinium ylides series.
Results and Discussion

In order to obtain new diazinium ylides derived from 3-\(p\)-halophenylpyridazine and 4-methylpyrimidine, the salts method of Kröhnke was used.\(^{11}\) Thus, N-carbalkoxy diazinium salts 4-9 were prepared by treating diazines with methyl and ethyl bromoacetate.\(^{12}\) The salts 4-9 in an aqueous solution of alkaline carbonates, afforded the corresponding diazinium carbalkoxy ylides 10, 11, 12, 14, 15, and unexpectedly, to a mixture ylide, 13-betaine 16, only in the case of salts 7, Scheme 1.

Diazinium carbalkoxy ylides 10-15, proved to be stable compounds, more stable than the diazinium-\(p\)-R-benzoylmethylides.\(^{10}\) The higher stability of these ylides could be explained through the convergent effect of two factors: the delocalization of ylide carbanion charge to the carbalkoxy groups as well as through the enol-betaine structures of these ylides, Scheme 2.

Scheme 1

Scheme 2. Canonical structures for 4-methylpyrimidinium charbalkoxy methylides.
Unexpectedly, in the case of salts 7, in addition to the ylide, 13, the betaine compound 16, was also formed (in a ratio ylide/betaine 30:70). The mechanism that we propose for this reaction can account for these experimental results. Thus, in this case, a part of ylide 13 are trapping atmospheric CO2, leading to betaine 16, Scheme 3. Analogous trapping reactions were found in related cases.3,13,14

Scheme 3

In order to check our hypothesis, we generate the ylide 13 (using an aqueous solution of alkaline carbonates), either in an inert atmosphere (under nitrogen) either with continuously bubbling CO2 in to the reaction medium. As expected, in first case the percentage of betaine 16 decreased from 70% (as resulted in normal conditions) to 5% while in the second case the percentage of betaine 16 increased from 70% to 85%.

The structure of the new compounds, ylides and betaine, has been proven through elemental (N%) and spectral (IR, 1H-NMR, MS) analysis as well as by chemical methods. If we consider compounds 13 and 16 as representatives for the series, the spectral analysis is the following:

In the IR spectrum of ylide 13 the most important signal is that of the ketone group at $\nu=1730$ cm$^{-1}$; in the IR spectrum of betaine 16 at $\nu=1555$ cm$^{-1}$ and at $\nu=1420$ and 1370 cm$^{-1}$ appears the bands corresponding to unsymmetrical respectively symmetrical vibrations of the CO$_2^-$ group (medium intensity). At $\nu=1550$ cm$^{-1}$ appear the band of ketone group from betaine.

In the 1H NMR spectrum of ylide 13 the most important signals are those one of the He (α-endocyclic) and Hf (ylidic) protons. The He proton appears around 11.00 ppm (doublet, J= 5.5 Hz) and Hf appears in the multiplet from 8.10-7.20 ppm. These protons appear at such high chemical shifts because of the deshielding effect of the positive nitrogen, and, in the case of the ylidic proton Hf has to be added the deshielding effect of the carbalkoxy group. In the 1H NMR spectrum of betaine 16 the most important signals are also, those of the He (α-endocyclic) and Hf (betaine) protons. The He proton appears around 10.10 ppm (d, J= 5.5 Hz) and Hf at 6.00 ppm (s); Hf appears at lower chemical shift by more that one ppm as compared with the ylide because this time Hf is an aliphatic proton (not ylidic).

The mass spectra also confirm the structure of the products. In the MS spectrum of ylide 13 the most important MS fragments are: 278 (1.5%, M$^+$, from $^{37}$Cl); 261 (BP, 100%) and 263 (29.1%) [the main fragmentation reaction: M$^+$-15(CH$_3$)]; another important fragmentation is on the Nylidic-Cylidic bond:190(28.69%), 192(13,2%) and 86(1.6%); fragmentation of the rest from
190 (substituted pyridazine) lead to: 155(25.37%, 190-Cl), 111(21.64%) and 113(6.29%)[190-C₆H₄Cl]; other relevant fragments: 179(1.9%), 165(27.61%), 76(7.37%), 73 (6.09%, COOEt).

In the MS spectrum of betaine 16 the most important MS fragments are: 322 (0.64%, M⁺, from ³⁷Cl); 136 (BP, 100%) and 111(2,1%), 113(0.47%), 73 (0.8%, COOEt) [the main fragmentation reaction: M⁺-{C₆H₄Cl + COOEt}]; fragmentation on the Nylidic-Cylidic bond:190(28.69%), 192(13,14%) and 130(0.64%); the α-fragmentation to the CO ester group: 249(3.04%, from ³⁷Cl) and 73 (6.09%, COOEt); other relevant fragments: 155(2.08%), 111(2,1%), 79(1,8%), 76(7.37%), 75(40.54%), 74 (6.09%).

In both compounds the peaks are separated by 2 units with a relative intensity 3:1.

All the remaining signals (IR, NMR) and fragments are in accordance with the expected structures.

Further we have carried out the reactions of ylides with the dipolarophile DMAD both to obtain further chemical evidence for their structure and to gain access to new azabicyclic compounds.

![Scheme 4](image)

**Scheme 4**

Thus, we treated ylides 13 and 15 (generated in situ from the corresponding cycloimmonium salts), with DMAD, when reactions occur as a [3+2] dipolar cycloaddition leading to the azabicyclic compounds 17 and 18, Scheme 4.
In the case of pyrimidinium carbalchoxy methylides the cycloaddition reaction could involve either the 2- or 6- position of the pyrimidine ring. However, position 6 is less electron-deficient than position 2, therefore it is more suitable for reaction with an electron-poor dipolarophile.

The structure of the new compounds was established by elemental (N) and spectral (IR, \(^1\)H-NMR) analysis. For instance, if we consider compound 18, in the \(^1\)H-NMR spectrum the most important signals are those of the H\(_1\), H\(_4\) and methyl H-atoms of COOCH\(_3\) groups. The H\(_1\)-atom resonated at \(\delta=10.41\) ppm (singlet, 1H) while H\(_4\)-atom resonated at \(\delta=8.02\) ppm (singlet, 1H), which excludes the cyclisation to the carbon between the two nitrogen atoms. The signal of the CH\(_3\) ester groups appear as non-equivalent at \(\delta=3.85\) ppm (singlet, 3H, CH\(_3\) from 6 position) and respectively at \(\delta=3.30\) ppm (singlet, 3H, CH\(_3\) from 5 position).

In conclusion, pyrimidinium- and pyridazinium carbalkoxy methylides prove to be stable compounds with the exception of 3-(\(p\)-chlorophenyl)pyridazinium carbethoxymethylide 12 which traps atmospheric CO\(_2\) leading to a ylide-betaine. A selective way to increase the yield of ylide or betaine has been found. The structure of ylides and betaine has been proven through elemental and spectral (IR, NMR, MS) analysis as well as by chemical methods. Pyrimidinium- and pyridazinium carbalkoxy methylides react with DMAD, when reactions occur as a [3+2] dipolar cycloaddition leading to the azabicyclic compounds.

**Experimental Section**

**General Procedures.** \(^1\)H NMR spectra were run on a Bruker 80 MHz spectrometer and were recorded in ppm downfield from an internal standard, SiMe\(_4\). The coupling constants are given in Hz. The mass spectra were recorded by electron impact. The IR spectra were recorded with a SPECORD-71 spectrometer in KBr. The melting points are uncorrected. Technical nitrogen has been employed (98%).

**General procedure to obtain diazinium ylides**
1. Salts (10 mmol) was dissolved in 50 ml water and treated with an aqueous solution of K\(_2\)CO\(_3\) 40% when the ylide was obtained. The product was filtered off under vacuum, washed with a large amount of water and dried under vacuum.
2. Salts (10 mmol) was dissolved in 50 ml water, than an aqueous solution of K\(_2\)CO\(_3\) 40% was added, dropwise in 10 min. (stirring, under nitrogen (for ylides) or CO\(_2\) (for betaines)). The product was filtered off under vacuum, washed with a large amount of water and dried under vacuum.

**3-\(p\)-Bromophenylpyridazinium carbethoxymethylide (10).** According to General Procedure 1 or 2. Dark red compound. Yield 92%, m.p. 145-147 °C. Anal. C\(_{13}\)H\(_{10}\)N\(_2\)O\(_2\)Br: N: Calcd. 9.12, Found 8.80. IR (KBr): v: 1730(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \(^1\)H NMR \(\delta\) : 11.00 (d, H\(_e\), J= 6.0), 8.50 (d, H\(_c\), J= 8.0), 8.05-7.20 (m, 6H: 2H\(_a\), 2H\(_b\), H\(_d\), H\(_f\)), 3.90 (s, 3H: CH\(_3\)).
3-\textit{p}-Chlorophenylpyridazinium carbmethoxymethylide (11). According to \textit{General Procedure 1} or 2. Orange compound. Yield 90\%, m.p. 132-135 °C. Anal. C\textsubscript{13}H\textsubscript{10}N\textsubscript{2}O\textsubscript{2}Cl: N: Calcd. 10.66, Found 10.30. \textit{IR} (KBr): ν: 1730(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 11.00 (d, H\text{e}, J= 6.0), 8.50 (d, H\text{c}, J= 8.0), 8.05-7.20 (m, 6H: 2H\text{a}, 2H\text{b}, H\text{d}, H\text{f}), 3.90 (s, 3H: CH\text{3}).

3-\textit{p}-Bromophenylpyridazinium carbethoxymethylide (12). According to \textit{General Procedure 1} or 2. Shining red compound. Yield 86\%, m.p. 150-152 °C. Anal. C\textsubscript{14}H\textsubscript{13}N\textsubscript{2}O\textsubscript{2}Br: N: Calcd. 8.72, Found 8.40. \textit{IR} (KBr): ν: 1735(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 11.00 (d, H\text{e}, J= 6.0), 8.45 (d, H\text{c}, J= 8.0), 8.05-7.20 (m, 6H: 2H\text{a}, 2H\text{b}, H\text{d}, H\text{f}), 4.50-4.10 (q, 2H\text{g}, J= 8.0), 1.40-1.15 (t, 3H\text{h}, J= 8.0).

3-\textit{p}-Chlorophenylpyridazinium carbethoxymethylide (13). According to \textit{General Procedure 2}. Red-orange compound. Yield 87\%, m.p. 136-138 °C. Anal. C\textsubscript{14}H\textsubscript{13}N\textsubscript{2}O\textsubscript{2}Cl: N: Calcd. 10.12, Found 9.85. \textit{IR} (KBr): ν: 1730(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 11.00 (d, H\text{e}, J= 6.0), 8.50 (d, H\text{c}, J= 8.0), 8.10-7.20 (m, 6H: 2H\text{a}, 2H\text{b}, H\text{d}, H\text{f}), 4.50-4.10 (q, 2H\text{g}, J= 8.0), 1.40-1.15 (t, 3H\text{h}, J= 8.0). MS- see the text.

4-Methylpyrimidinium carbethoxymethylide (14). According to \textit{General Procedure 1} or 2. Pink compound. Yield 72\%, m.p. 130-132 °C. Anal. C\textsubscript{8}H\textsubscript{10}N\textsubscript{2}O\textsubscript{2}: N: Calcd. 16.86, Found 16.20. \textit{IR} (KBr): ν: 1730(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 8.95 (s, H\text{a}), 8.55-8.40 (d, H\text{c}, J= 6.0), 7.40-7.20 (m, 2H: H\text{b}, H\text{d}), 3.90 (s, 3H: CH\text{3} from COOCH\text{3}), 2.65 (s, 3H: CH\text{3} from 3 position).

4-Methylpyrimidinium carbethoxymethylide (15). According to \textit{General Procedure 1} or 2. Reddish compound. Yield 65\%, m.p. 123-125 °C. Anal. C\textsubscript{9}H\textsubscript{12}N\textsubscript{2}O\textsubscript{2}: N: Calcd. 15.55, Found 15.20. \textit{IR} (KBr): ν: 1730(s), 1600, 1500, 1470, 1400 (s-m), 1235, 1125(s-m), 2950 (w), 3100-3000(w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 8.95 (s, H\text{a}), 8.55-8.40 (d, H\text{c}, J= 6.0), 7.40-7.20 (m, 2H: H\text{b}, H\text{d}), 4.50-4.15 (q, 2H\text{g}, J= 8.0), 1.35-1.20 (t, 3H\text{h}, J= 8.0), 2.65 (s, 3H: CH\text{3} from 3 position).

3-\textit{p}-Chlorophenylpyridazinium carboxyacetate (16). According to \textit{General Procedure 2}. Reddish compound. Yield 67\%, m.p. 115-117 °C. Anal. C\textsubscript{15}H\textsubscript{13}N\textsubscript{2}O\textsubscript{4}Cl: N: Calcd. 8.73, Found 8.45. \textit{IR} (KBr): ν: 1750(s), 1550, 1420, 1370(s-m), 1600, 1510, 1400 (s-m), 1235, 1100(s-m), 2950 (w). \textit{\textit{\textit{^1\textit{H NMR}}} δ : 10.10 (d, H\text{c}, J= 6.0), 9.00 (d, H\text{c}, J= 8.0), 8.70 (t, H\text{e}, J= 8.0, J= 6.0), 6.00 (s, H\text{f}), 8.00-7.20 (m, 4H: 2H\text{a}, 2H\text{b}), 4.50-4.15 (q, 2H\text{g}, J= 8.0), 1.30-1.15 (t, 3H\text{h}, J= 8.0). MS- see the text.

General procedure to obtain 3+2 cycloadducts
The cycloimmonium salt(2 mmol) and DMAD(2 mmol) were suspended in 20 ml of benzene. The mixture was heated for 2 h on a steam bath and triethylamine (2 mmol, dissolved in 3 ml benzene) was added dropwise (in 30 min.). The resulting mixture was filtered hot, to eliminate triethylamine bromhydrate. The clear solution was evaporated on a steam bath. The crude products recrystallized from acetone for compound 17, and for compound 18 we done flash chromatography on silica using dichloromethane-methanol 99:1.
5,6-Dicarbomethoxy-2-(4-chlorophenyl)-7-carbethoxypyrrrolo[1,2-b]pyridazine (17). Dark cream compound. Yield 76%, m.p. 81-83 °C. Anal. C_{20}H_{17}N_{2}O_{6}Cl: N: Calcd. 6.72, Found 6.30. IR (KBr, cm⁻¹): ν: 1745,1720(s, 1650, 1600, 1560, 1460 (s-m), 1230, 1130(s-m), 2950 (w), 3100-3000(w). \(^1\)H NMR δ: 8.80-8.60 (d, H₃, J= 9.0), 7.80-7.30 (m, 5H: 1H₄, 4H[-C₆H₄-]), 4.30-4.15 (q, 2H[CH₂], J= 8.0), 3.85 (s, 3H: CH₃ from 6 position), 3.70 (s, 3H: CH₃ from 5 position), 1.40-1.10 (t, 3H[CH₃], J= 8.0).

5,6-Dicarbomethoxy-3-methyl-7-carbethoxypyrrrolo[1,2-c]pyrimidine (18). Redish liquid. Yield 46%. \(^1\)H NMR δ: 10.41 (s, H₁), 8.02 (s, H₄), 4.10-3.80 (m, 2H[CH₂]), 3.85 (s, 3H: CH₃ from 6 position), 3.30 (s, 3H: CH₃ from 5 position), 1.30-1.20 (t, 3H[CH₃], J= 8.0), 2.70 (s, 3H: CH₃ from 3 position).

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References