Ketenes from \textit{N}-(2-Pyridyl)amides. Isolation of Methoxycarbonyl Ketenes

Carsten Plüg and Curt Wentrup*

Department of Chemistry, The University of Queensland, Brisbane, QLD 4072, Australia

The elimination of \(\text{HX} \ (\text{X} = \text{Cl}, \text{OR}, \text{OAc}, \text{etc.})\) from carboxylic acid derivatives under conditions of flash vacuum thermolysis (FVT) is a useful means of generation of ketenes.\(^3\) The FVT of \(N\)-acylpyrazoles at 575–750°C belongs to this class of reactions.\(^2,3\) However, the usefulness of this method is limited by the mostly extreme moisture sensitivity of the pyrazolidine starting materials and the relatively high pyrolysis temperatures required. For example, we have recently generated and characterized the highly reactive cyanoketene by FVT of cyanoacetic acid derivatives, including the pyrazolidine, but none of these reactions were complete until 700–850°C as determined by matrix isolation infrared spectroscopy and on-line tandem mass spectrometry.\(^3\)

Here, we report that FVT of the stable, moisture-insensitive, and easily prepared 2-pyridylamides such as \(2\) is a highly efficient alternative, giving high yields of methoxycarbonylketenes \(3\) under relatively mild FVT conditions (ca. 480°C).

The \(N\)-(2-pyridyl)malonamides \(2\) were readily prepared by condensation of methyl malonate with 2-(methylamino)pyridine (1) with the aid of dicyclohexylcarbodiimide. They were fully characterized on the basis of their \(^1\)H and \(^13\)C NMR, IR, and mass spectra and elemental analyses. On FVT at 480°C with \(\text{Ar}\) matrix isolation\(^4\) of the product mixtures at 14 K, the formation of the methoxycarbonylketenes \(3\) together with the regenerated amine 1 was observed by FTIR spectroscopy (Table 1). The bands due to the amine 1 (not tabulated) in this spectrum were identical with those of authentic 1 deposited with \(\text{Ar}\) at 14 K from a reservoir at room temperature. It is known from previous work that the 2-amino form is far more stable than the 2-imine tautomer, especially in the gas phase, but also in solution.\(^5\)

While on FVT of amide \(2a\), formation of small amounts of \(\text{C}_2\text{O}_2\)\(^6\) and methanol was observed, no

\begin{table}
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\begin{tabular}{|c|c|c|c|}
\hline
& \(3\) & \(3a\) & \(3b\) \\
\hline
2964 (w) & 2967 & 2966 & 2144 (vs) \\
2156 (s) & 2156 & 2156 & 2142 (s) \\
2152 (vs) & 2152 & 2152 & 2136 (m) \\
2149 (m) & 2149 & 2149 & 2130 (m) \\
1746 (s) & 1747 & 1747 & 1739 (s) \\
1719 (m) & 1719 & 1719 & 1729 (m) \\
1441 (m) & 1441 & 1441 & 1721 (m) \\
1391 (m) & 1391 & 1391 & 1296 (s) \\
1364 (m) & 1354 & 1355 (sh) & 1290 (s) \\
1238 (s) & 1238 & 1238 & 1194 (m) \\
1199 (m) & 1200 & 1200 & 1137 (s) \\
1184 (m) & 1184 & 1184 & 746 (w) \\
934 (v/v) & 934 & 934 & 731 (w) \\
849 (v/v) & 849 & 849 & 849 \\
756 (m) & 757 & 757 & \\
\hline
\end{tabular}
\caption{IR data (Ar, 14 K, in cm\(^{-1}\)) for methoxycarbonylketene (3a) formed from precursors 2a (480°C), 4 (520°C) and 5 (420°C), and methoxycarbonylmethylketene (3b) formed from 2b (480°C).}
\end{table}

detectable by-products were formed from \(2b\) under the same conditions (480°C). When the thermolyses were performed at lower temperatures, some starting material (2) was present in the product mixtures in both cases.

\*To whom correspondence should be addressed.
although substantial amounts of ketenes 3 were formed even at 380 °C. Thermolysis of 2a at temperatures above 480 °C caused a dramatic increase in the relative intensities of the bands due to C₃O₂; thus, on FVT at 820 °C, the C=C=O bands of ketene 3a and the major bands of C₃O₂ had the same intensity. However, there was no other significant change in the spectrum, ketene 3a still being produced quite cleanly. FVT of 2b at 820 °C caused partial decomposition with the formation of new bands in the IR spectrum, but ketene 3b was still the major product. The new species formed is not dimethylketene or 1-methoxypropyne, both of which are known compounds. The Ar matrix IR spectrum of the former has been reported previously, and a sample of the latter was prepared by a known method for direct comparison.

When the thermolysis products from 2a (480 °C) were trapped at liquid N₂ temperature (−196 °C; neat) and subsequently allowed to warm up, regeneration of amide 2a was observed by difference IR spectroscopy at approximately −130 °C, thereby providing good evidence for the structure of the ketene.

In view of the above success, we reexamined the FVT of dimethyl malonate (4), from which we had previously obtained low quality Ar matrix IR spectra. FVT of 4 at 520 °C produced mainly the unchanged starting material. In addition, weak bands due to C₃O₂, CO₂, and ketene 3a were obtained. Higher pyrolysis temperatures caused an increase in the ratio of the bands due to ketene 3a and those due to the starting material, as well as increased CO₂ and C₃O₂ formation. As indicated in Table 1, it is possible to detect all the bands due to ketene 3a, but the procedure is far less efficient and the spectrum of much poorer quality than the one resulting from FVT of 2a: although the decomposition of 4 was far from complete at 520 °C, the ratio of intensities of the bands due to 3a and C₃O₂ was already ca. 2.7:1 (compared with 7:1 using 2a as precursor at 480 °C).

The pyrazoline 5 was prepared as an alternative precursor for ketene 3a using DCC-mediated condensation of monomethyl malonate with 3,5-dimethylpyrazole by analogy with the procedure employed for 2. Compound 5 is highly sensitive to moisture, and the spectra indicated that partial hydrolysis had taken place. Nevertheless, FVT at 420 °C permitted identification of most of the IR bands due to 3a in the Ar matrix spectrum (Table 1), but the reaction was very incomplete.

Ketene 3a has been generated previously by FVT of methyl 3-methoxy-3-trimethylsilyloxy-2-propenoate (loss of methyl trimethylsilyl ether). The ketene was detected by on-line mass spectrometry and substantiated by isolation of a dimer and of trapping products, but it was not spectroscopically observable at −80 °C. Intermediacy of ketene 3b has been postulated in the reaction of ethyl 2-(chlorocarbonyl)propiionate with triethylamine. The ketene was detected by means of a gas-phase IR band at 2157 cm⁻¹ on decomposition of the requisite 2-oxo-butane dioic ester in the hot light-pipe of a GC-IR instrument. However, none of these methods have permitted the isolation or detailed characterization of the ketenes.

In conclusion, the thermal elimination of 2-(methylamino)pyridine (1) from amides 2 generates the methoxy carbonylketenes 3. This methodology has advantages over other ketene-producing reactions in that the starting materials 2 are stable and non-hygrosopic; the reactions take place under relatively mild FVT conditions, and the spectral purity of the ketenes obtained is excellent. This method should be applicable to the synthesis of many other types of ketene, and the scope will be the subject of further investigation. Experimental details as well as density functional calculations of the IR spectra of the s-cis and s-trans forms of ketenes 3, and of the tautomeric forms of 1, will be published in the full paper.

Acknowledgements. This work was supported by the Australian Research Council.

References


Received October 10, 1997.