

Letter

Ketenes from *N*-(2-Pyridyl)amides. Isolation of Methoxycarbonyl Ketenes

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The elimination of HX (X=Cl, OR, OAc, etc.) from carboxylic acid derivatives under conditions of flash vacuum thermolysis (FVT) is a useful means of generation of ketenes.¹ 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 pyrazolide 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 pyrazolide, 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

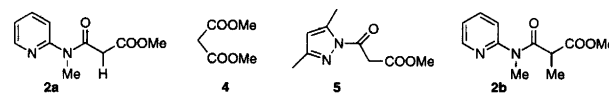
Here, we report that FVT of the stable, moisture-insensitive, and easily prepared 2-pyridylamides such as **2** is a highly efficient alternative, giving high yields of alkoxyketenes **3** under relatively mild FVT conditions (ca. 480 °C).

The *N*-(2-pyridyl)malonylamides **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 ¹H and ¹³C NMR, IR, and mass spectra and elemental analyses. On FVT at 480 °C with Ar matrix isolation⁴ 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 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 C₃O₂⁶ and methanol was observed, no

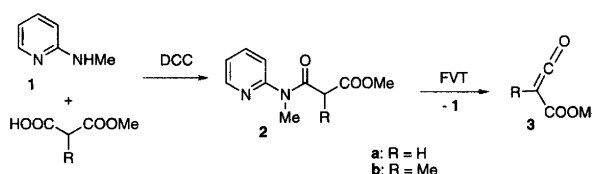
Table 1. IR data (Ar, 14 K, in cm⁻¹) for methoxycarbonylketene (**3a**) formed from precursors **2a** (480 °C), **4** (520 °C) and **5** (420 °C), and methoxycarbonyl(methyl)ketene (**3b**) formed from **2b** (480 °C).

Precursor:



Ketene:

3a	3a	3a	3b
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)
1354 (m)	1354	1355 (sh)	1290 (s)
1238 (s)	1238	1238	1194 (m)
1199 (m)	1200	1200	1137 (s)
1184 (m)	1184		746 (w)
934 (vw)	934	934	731 (w)
849 (vw)	849		
756 (m)	757		



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,

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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,⁷ and a sample of the latter was prepared by a known method⁸ 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.⁷ 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 pyrazolide **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).⁸ 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.⁸ Intermediacy of ketene **3b** has been postulated in the reaction of ethyl 2-(chlorocarbonyl)propionate with triethylamine.⁹ The ketene was detected by means of a gas-phase IR band at 2137 cm^{−1} on decomposition of the requisite 2-oxobutanedioic ester in the hot light-pipe of a GC-IR instrument.¹⁰ 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 methoxycarbonylketenes **3**. This methodology has advantages over other ketene-producing reactions in that the starting materials **2** are stable and non-hygroscopic; 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.¹¹

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References

- (a) Tidwell, T. T. *Ketenes*, Wiley, New York 1995; (b) Wentrup, C., Heilmayer, W. and Kollenz, G. *Synthesis* (1994) 1219.
- Besida, J., Brown R. F. C., Colmanet, S. and Leach, D. N. *Aust. J. Chem.* 35 (1982) 1373.
- Moloney, D. J. W., Wong, M. W., Flammang, R. and Wentrup, C. *J. Org. Chem.* 62 (1997) 4240; Flammang, R., van Haverbeke, Y., Wong, M. W., Rühmann, A. and Wentrup, C. *J. Phys. Chem.* 98 (1994) 4814.
- Kappe, C. O., Wong, M. W. and Wentrup, C. *J. Org. Chem.* 60 (1995) 1686; Wentrup, C., Blanch, R., Briehl, H. and Gross, G. *J. Am. Chem. Soc.* 110 (1988) 1874.
- Elguero, J., Marzin, C., Katritzky, A. R. and Linda, P. *The Tautomerism of Heterocycles*, Academic Press, New York 1976.
- Maier, G. and Rohr, C. *Liebigs Ann. Chem.* (1996) 307; Smith, W. H and Leroi, G. E. *J. Phys. Chem.* 45 (1966) 1767; Ohana, T. and Yabe, A. *Chem. Lett.* (1996) 325.
- Leung-Toung, R. and Wentrup, C. *Tetrahedron* 48 (1992) 7641.
- Jullien, J., Pechine, J. M. and Perez, F. *Tetrahedron Lett.* 24 (1983) 5525.
- Ficini, J. and Pouliquen, J. *Tetrahedron Lett.* (1972) 1135.
- Emerson, D. W., Titus, R. L. and Gonzalez, R. M. *J. Org. Chem.* 56 (1991) 5301.
- Plüg, C., Wong, M. W. and Wentrup, C. *Unpublished results.*

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