Synthetic Methods

DOI: 10.1002/anie.201412431

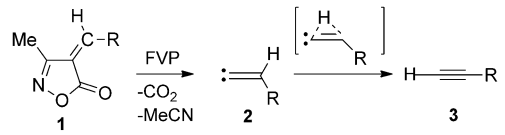
Falling-Solid Flash Vacuum Pyrolysis: An Efficient Preparation of Arylacetylenes**

Curt Wentrup, Jürgen Becker, and Hans-Wilhelm Winter*

Dedicated to Professor Fritz Vögtle on the occasion of his 75th birthday

Abstract: *Automated falling-solid flash vacuum pyrolysis allows the rapid and efficient synthesis of a variety of arylacetylenes from 4-arylmethylidene-5(4H)-isoxazolone derivatives, which were prepared from aldehyde precursors. The acetylenes are readily obtained in multigram quantities.*

The popularity of click chemistry[1] has sparked renewed interest in the synthesis of acetylenes. Flash vacuum pyrolysis (FVP) of 4-methyleneisoxazol-5(4*H*)-ones **1**, readily synthesized from 3-methylisoxazolone and aldehydes, gives access to a variety of alkynes **3** in high yields (Scheme 1).[2] Details of the mechanism of the reaction have been investigated computationally,[3] and it has been found to take place via



Scheme 1. Synthesis of acetylenes **3** by FVP of isoxazolones **1**.

transient ethynylidenes **2**, which by 1,2-hydrogen migration afford the acetylenes **3**. This reaction and its reverse, the acetylene–vinylidene rearrangement, are of considerable theoretical interest.[4] Analogous FVP of 4-aminomethyleneisoxazolones allowed the generation and characterization of ethynylamines RR′N–C≡C–H and RNH–C≡C–H and ketenimines R–N=C=CH_2.[5]

However, numerous compounds are too involatile for conventional FVP.[6,7] For this reason, various methods such as solvent-spray[8] and solid-pyrolysis[9] procedures have been employed. We have developed a fully automated, convenient, controllable, and rapid falling-solid flash vacuum pyrolysis (FS-FVP), in which the finely powdered, solid starting material is added in a continuous manner to a vertical pyrolysis tube under high vacuum (Figure 1). The crucial and innovative centerpiece is the spinning brush (E), which permits the controlled addition of the starting material into the vertical pyrolysis tube as a steady spray of powdered solid. Commercially available, tight-fitting spiral bottle brushes with nylon 6,6 bristles work very well. The amount of sample per unit time is easily controlled by the velocity of the spinning brush. To prevent the solid from falling through the tube unchanged, a fine plug of quartz wool is suspended on top of a quartz cross in the center of the pyrolysis tube.

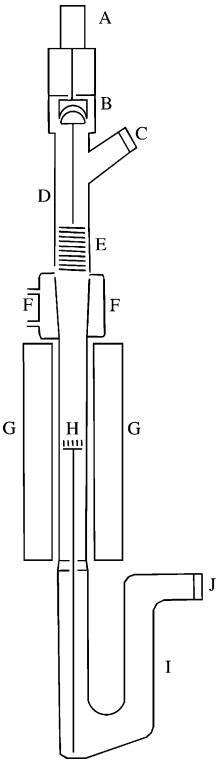


Figure 1. Automated apparatus for falling-solid flash vacuum pyrolysis (FS-FVP). A) spinning-band motor; B) magnetic coupling; C) sample refill port; D) sample compartment; E) tight-fitting rotating brush attached to drive shaft above; F) water-cooled mantle; G) electrical pyrolysis oven housing a 30×2 cm quartz pyrolysis tube; H) quartz wool supported on a quartz rod ending with a cross and standing in the cold trap; I) cold trap; J) connection to second cold trap and high vacuum system. The sample is placed on top of the brush E before applying vacuum and starting the operation. A pressure-equalizing side tube connects the top and bottom of the sample and brush compartments (not shown).

[*] Prof. Dr. C. Wentrup
School of Chemistry and Molecular Biosciences
The University of Queensland
Brisbane, Qld 4072 (Australia)
E-mail: wentrup@uq.edu.au
Prof. Dr. C. Wentrup, Dr. J. Becker, Dr. H.-W. Winter
Fachbereich Chemie der Philipps-Universität
35037 Marburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Australian Research Council.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201412431.

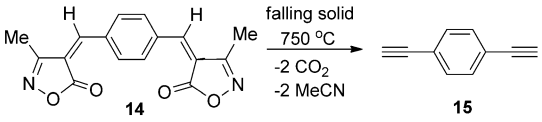
Alternatively, if the pyrolysis tube is held slightly nonvertically, the solid will fall and volatilize on the hot wall. To minimize vacuum fluctuations, it is preferable to insert an 8 L (or larger) vacuum ballast in the high-vacuum pumping line. We report herein the employment of this apparatus in the synthesis of acetylenes. Other examples will be summarized below.

The isoxazolone starting materials **6** described below are too involatile for efficient FVP under conventional conditions. In contrast, the falling-solid pyrolysis is rapid, can be conducted easily on a multigram scale, and generally affords high yields. Being a continuous flow method, it is possible to scale up the reaction to much larger quantities. Employing this technique, we have prepared several tens of grams of acetylenes. The isoxazolones **6** (Scheme 2) were synthesized from 3-methylisoxazolone (**4**) and the appropriate aldehyde **5** using a previously reported procedure.[2]

The synthesis of the *p*-nitrobenzylidene isoxazolone **9** took an unexpected course. In fact, the product of reaction of 3-methylisoxazolone (**4**) with *p*-nitrobenzaldehyde was the bis(isoxazolyl)methane derivative **8**, which is far too involatile for conventional FVP. However, falling-solid pyrolysis of **8** at 750 °C afforded **10** in 71 % yield (Scheme 2). During the course of this reaction 3-methylisoxazolone (**4**) is eliminated, thus generating **9**, which subsequently undergoes pyrolysis to form **10**. The eliminated 3-methylisoxazolone undergoes pyrolysis to form 2-methyl-1-azirine, as we have described for the analogous formation of 2-phenyl-1-azirine,[10] but under these reaction conditions the azirine decomposes to form HCN and ethene.

Similarly, 2-phenylbenzaldehyde reacted with two molecules of 3-methylisoxazolone (**4**) to yield compound **11**. Falling-solid pyrolysis of **11** at 700 °C afforded 2-biphenylylacetylene (**13**) in 65 % yield. Phenanthrene[4] was also isolated from this reaction in 12 % yield together with a trace of benz[*a*]azulene.

For a further proof of principle, 1,4-diethynylbenzene (**15**) was prepared in 72 % yield by falling-solid FVP of the highly involatile 1,4-phenylenebis(methyleneisoxazolone) (**14**) at 750 °C (Scheme 3).

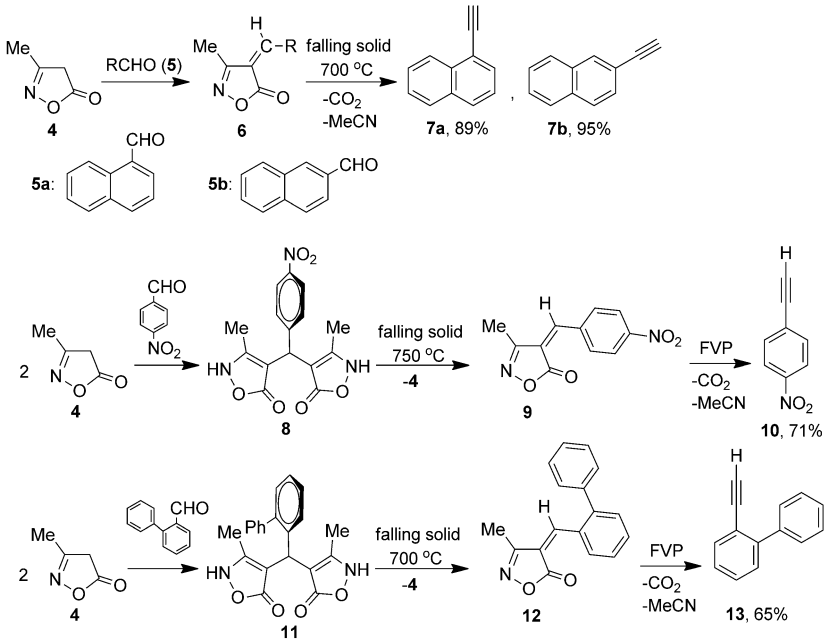


Scheme 3. Preparation of 1,4-diethynylbenzene (**15**) by FS-FVP.

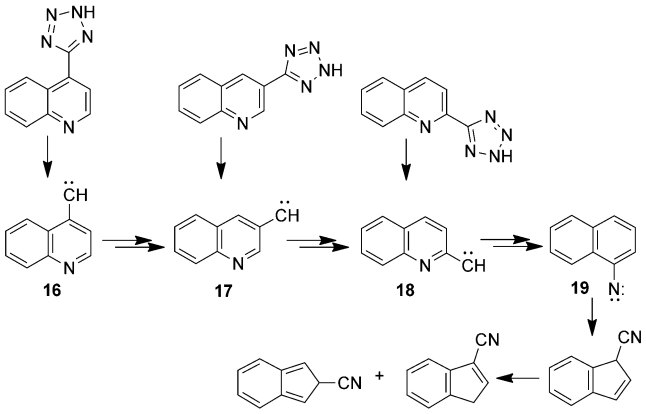
We have used the same method to synthesize a variety of aryl- and heteroarylacetylenes prepared previously by conventional FVP.[2] The great advantage of the FS-FVP method is that multigram quantities can be obtained in a few hours. For the reactions shown in Scheme 2 and 3, the falling-solid method is far superior.

The falling-solid pyrolysis method is advantageous in many other applications. For example, 5-substituted tetrazoles are convenient and safe starting materials for the pyrolytic generation of arylcarbenes,[11] but they are often too involatile to be practical. Here, we have used FS-FVP to generate the 4- and 3-quinolylcarbenes **16** and **17** (Scheme 4). Both carbenes undergo rearrangement to form 2-quinolylcarbene (**18**; also generated from the tetrazole) and then to 1-naphthylnitrene (**19**), which finally undergoes ring contraction to form 1-cyanoindene and then 3- and 2-cyanoindenes. Similarly, both the tetrazole and the aldehyde tosylhydrazone sodium salt have been used to generate 1-azulenylcarbene (**20**), which rearranges to form cyclobuta[*de*]naphthalene (**21**) and cyclopenta[*cd*]indene (**22**; Scheme 5). Experimental details of these reactions and elucidation of the reaction mechanisms will be published elsewhere. Although the thermal decomposition of tosylhydrazone salts has been employed for the generation of volatile diazo compounds, this method fails or else affords only very poor yields for compounds with more than about ten heavy atoms. This is a result of decreased volatility, which results in uncontrolled decomposition of the diazo compounds under conventional FVP conditions.

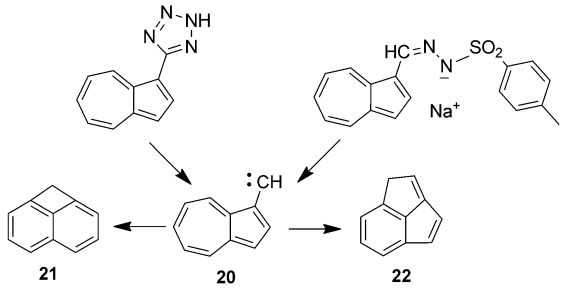
In conclusion, falling-solid flash vacuum pyrolysis enables the use of involatile starting materials in FVP reactions. Applied to 4-arylmethyleneisoxazolone starting materials, it is an extremely useful technique for the gram-scale preparation of arylacetylenes.



Scheme 2. Aryl acetylenes prepared by falling-solid flash vacuum pyrolysis (FS-FVP). Preparative yields on a 1–5 g scale are given (%).



Scheme 4. Generation of quinolylcarbenes by FS-FVP of tetrazoles.



Scheme 5. Generation of 1-azulenylcarbene (**20**) by FS-FVP of the tetrazole and aldehyde tosylhydrazone sodium salt.

Experimental Section

Standard procedure for the preparation of arylacetylenes by falling-solid flash vacuum pyrolysis: The relevant isoxazolone (2.0 g) was loaded on top of the tight-fitting brush in the falling-solid pyrolysis apparatus. Upon application of the vacuum, the pyrolysis oven was brought to the required temperature (typically 750 °C). The cold trap was immersed in liquid N_2 (employing usually two cold traps in series). The spinning-band motor was started, and the pyrolysis took place over the course of 2.5 h, typically at a dynamic pressure of 10^{-3}–10^{-1} hPa. After the pyrolysis, CO_2 and acetonitrile were removed under vacuum, and the product was isolated from the cold trap by dissolution (e.g. in CH_2Cl_2) or distillation.

Received: December 28, 2014
Revised: January 26, 2015
Published online: ■■ ■■, ■■■■

Keywords: alkynes · arenes · flash pyrolysis · rearrangement · synthetic methods

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Communications

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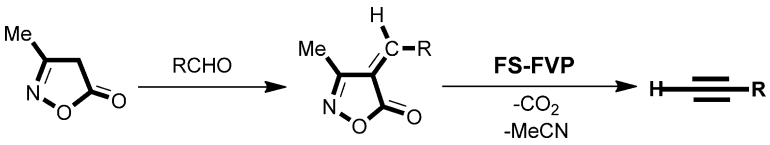
C. Wentrup,* J. Becker,
H.-W. Winter ——— ▮▮▮▮–▮▮▮▮



Falling-Solid Flash Vacuum Pyrolysis: An Efficient Preparation of Arylacetylenes

Taking the heat: Unlike in flash vacuum pyrolysis, involatile compounds can be used in falling-solid flash vacuum pyrolysis (FS-FVP). This method is employed for the rapid and efficient synthesis of a variety of arylacetylenes from 4-arylmethylidene-5(4*H*)-isoxazolones, which were in turn prepared from aldehyde precursors.

