JOC*Note*

High-Speed Microwave-Promoted Hetero-Diels−Alder Reactions of 2(1*H*)-Pyrazinones in Ionic Liquid Doped Solvents

Erik Van der Eycken,*[,†] Prasad Appukkuttan,[†] Wim De Borggraeve,[†] Wim Dehaen,[†] Doris Dallinger,[‡] and C. Oliver Kappe*[,‡]

Laboratory for Organic Synthesis, Katholieke Universiteit Leuven, Celestijnenlaan 200F, B-3001 Heverlee, Belgium, and Institute of Chemistry, Karl-Franzens-University Graz, Heinrichstrasse 28, A-8010 Graz, Austria

erik.vandereycken@chem.kuleuven.ac.be; oliver.kappe@uni-graz.at

Received August 14, 2002

Abstract: Inter- and intramolecular hetero-Diels−Alder reactions in a series of functionalized 2(1*H*)-pyrazinones were investigated under controlled microwave irradiation. The cycloaddition reactions were efficiently performed in sealed tubes, utilizing either a combination of 1,2-dichloroethane and a thermally stable ionic liquid, or 1,2-dichlorobenzene as reaction medium. In all cases, a significant rate-enhancement using microwave flash heating as compared to thermal heating was observed.

The readily accessible and broadly functionalized 2-azadiene system of the 2(1*H*)-pyrazinone scaffold[1] has been shown to offer unique opportunities for inter- and intramolecular cycloaddition reactions with electron-rich and electron-poor dienophiles.[2] It has been demonstrated, for example, that pharmacologically interesting compounds containing a β-carbolinone or α-carboline skeleton can be synthesized starting from 2(1*H*)-pyrazinone precursors via an intramolecular cycloaddition−elimination sequence.[3] Starting from alkenylpyrazinones, the tricyclic core skeleton of the brevianamides natural products could be synthesized via an intramolecular cycloaddition route.[4] The construction of novel types of conformationally restricted dipeptide analogues as β-turn mimetics via intermolecular cycloaddition of these heterodienes with ethene has also been reported recently.[5] Although 2(1*H*)-pyrazinones are interesting heterodienes and therefore versatile building blocks for the generation of a number of important product classes, their cycloaddition chemistry suffers from some inconveniences. In many cases rather long reaction times at high temperatures and sometimes high pressures are required to successfully perform these hetero-Diels−Alder cycloadditions, restricting the practical synthetic utility of this chemistry.

In recent years, the concept of speeding up synthetic transformations by microwave activation has created a lot of interest in the organic[6] and combinatorial chemistry community.[7] In particular, the use of dedicated microwave reactors that enable the rapid and safe heating of reaction mixtures in sealed vessels under controlled conditions with on-line temperature and pressure monitoring has greatly increased the general acceptance of the microwave heating method. A very recent trend in this area is to use ionic liquids, or mixtures of ionic liquids and comparatively unpolar solvents, as reaction media in microwave-heated transformations.[8−11] Due to their ionic nature, ionic liquids couple very effectively with microwaves through an ionic conduction mechanism.[9] Therefore, small amounts of an ionic liquid can be employed as additives in order to increase the dielectric constant of an otherwise nonpolar solvent medium.[9] In addition, ionic liquids are also known to mediate or enhance a number of important synthetic transformations, including Diels−Alder cycloaddition reactions.[12]

It therefore appeared to us that a microwave/ionic liquid strategy would be ideally suited to apply to both inter- and intramolecular cycloaddition reactions involving the 2(1*H*)-pyrazinone scaffold. The hetero-Diels−Alder reactions in this series are known to be rather sluggish, with reaction times of many hours or even days being quite common.[2−5] In an attempt to make those valuable synthetic transformations more useful and applicable to a high-throughput format, we have explored the potential rate-enhancements by microwave irradiation in the presence of ionic liquids.

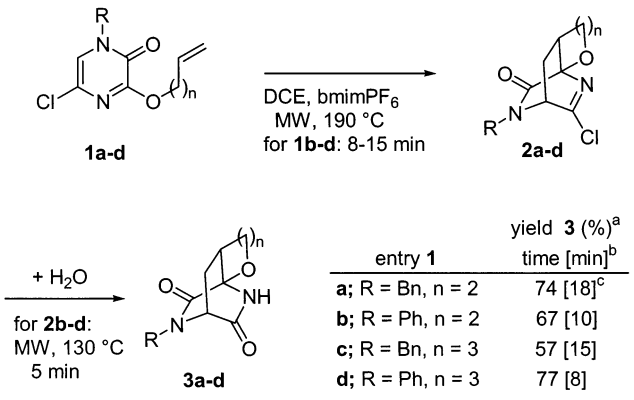
Our starting point in these investigations involved intramolecular hetero-Diels−Alder reactions in a series of alkenyl-tethered 2(1*H*)-pyrazinones **1a**−**d** (Scheme 1). Under conventional thermal conditions, reaction times of 1−2 days have been reported for those types of cycloaddition processes (**1** → **2**) involving chlorobenzene as solvent under reflux conditions (132 °C).[4] Our initial microwave experiments were performed with pyrazinone **1a** as a model substrate involving distilled 1,2-dichloroethane (DCE) as solvent. DCE has been utilized successfully in microwave-assisted chemistry before,[6] has a considerably lower boiling point (83 °C) than chlorobenzene (132 °C), and is therefore easier to work with. The loss-tangent (tan δ) of DCE—governing the ability of the solvent to couple with 2.45 GHz microwave irradiation—is similar to that of water (tan δ at 20 °C: DCE 0.127; H_2O 0.123).[13] Therefore, DCE couples with microwaves

[†] Katholieke Universiteit Leuven.
[‡] Karl-Franzens-University Graz.

(1) Vekemans, J.; Pollers-Wieërs, C.; Hoornaert, G. *J. Heterocycl. Chem.* **1983**, 919−923.
(2) Hoornaert, G. *Bull. Soc. Chim. Belg.* **1994**, *103*, 583−589.
(3) Tahri, A.; Buysens, K. J.; Van der Eycken, E. V.; Vandenberghe, D. M.; Hoornaert, G. J. *Tetrahedron* **1998**, *54*, 13211−13226.
(4) De Borggraeve, W. M.; Rombouts, F. J. R.; Verbist, B. M. P.; Van der Eycken, E. V.; Hoornaert, G. J. *Tetrahedron Lett.* **2002**, *43*, 447−449.
(5) De Borggraeve, W. M.; Rombouts, F. J. R.; Van der Eycken, E. V.; Toppet, S. M.; Hoornaert, G. J. *Tetrahedron Lett.* **2001**, *42*, 5693−5695.
(6) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225−9283.
(7) (a) Lew, A.; Krutzik, P. O.; Hart, M. E.; Chamberlin, A. R. *J. Comb. Chem.* **2002**, *4*, 95−105. (b) Kappe, C. O. *Curr. Opin. Chem. Biol.* **2002**, *6*, 314−320.
(8) Varma, R. S.; Namboodiri, V. V. *Chem. Commun.* **2001**, 643−644.
(9) Leadbeater, N. E.; Torenius, H. M. *J. Org. Chem.* **2002**, *67*, 3145−3148.
(10) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. *Org. Lett.* **2002**, *4*, 1567−1570.
(11) Vallin, K. S. A.; Emilsson, P.; Larhed, M.; Hallberg, A. *J. Org. Chem.* **2002**, *67*, 6243−6246.
(12) (a) Fischer, T.; Sethi, A.; Welton, T.; Woolf, J. *Tetrahedron Lett.* **1999**, *40*, 793−796. (b) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, *1*, 23−25.

10.1021/jo0263216 CCC: $22.00
Published on Web 10/04/2002

SCHEME 1[a]



entry **1**	yield **3** (%)[a] time [min][b]
a; R = Bn, n = 2	74 [18][c]
b; R = Ph, n = 2	67 [10]
c; R = Bn, n = 3	57 [15]
d; R = Ph, n = 3	77 [8]

[a] (a) Isolated yield of **3**. (b) Time needed for conversion of **1** to **2**. (c) Time needed for conversion of **1a** to **3a** as spontaneous hydrolysis of **2a** occurred during the reaction.

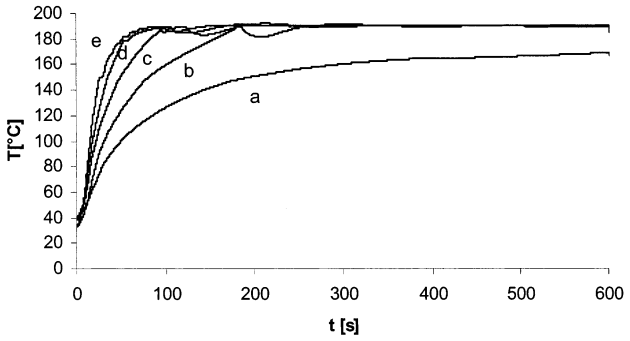


FIGURE 1. Heating profiles for microwave-heated DCE (300 W maximum power, 190 °C preselected maximum temperature) doped with varying amounts of 1-butyl-3-methylimidazolium hexafluorophosphate (bmimPF_6). Experiments were carried out in a 5 mL sealed microwave process vial (ref 14) containing 2 mL of DCE. Profile a: neat DCE. Profile b: 0.035 mmol of bmimPF_6. Profile c: 0.075 mmol of bmimPF_6. Profile d: 0.150 mmol of bmimPF_6. Profile e: 0.300 mmol of bmimPF_6. Temperatures were recorded on the outer surface of the glass vial by an IR sensor.

reasonably well, leading to the heating profile displayed in Figure 1 when irradiated in a single-mode microwave cavity (profile a).[14] Using a preselected maximum temperature of 190 °C (300 W maximum power), neat DCE can be heated to ca. 170 °C within 10 min under sealed vessel conditions. No further increase of the temperature (i.e., to the preselected setting of 190 °C) could be observed on prolonged heating. Under these conditions, the complete conversion of **1a** took ca. 50 min, which represents a considerable shortening of the reaction time as compared to the 1−2 days required under the conventional chlorobenzene reflux conditions. Note that in contrast to heating the neat solvent (DCE, profile a), the solution of **1a** in DCE reached the 170 °C temperature more rapidly (within ca. 3 min, profile not shown), indicating that the 2(1*H*)-pyrazinone is acting as a "molecular radiator",[15] itself absorbing some of the microwave energy. In an effort to further enhance the maximum attainable reaction temperature (and therefore shortening the reaction time) we have doped the solvent with varying amounts of a room-temperature ionic liquid (Figure 1, profiles b−e). Based on a very recent study on the thermal stability of a variety of ionic liquids/solvent combinations under high-temperature microwave conditions,[9] we have selected 1-butyl-3-methylimidazolium hexafluorophosphate (bmimPF_6) as the ionic liquid of choice for our investigations. Adding 0.035 mmol of bmimPF_6 to the neat solvent (2 mL of DCE) the preselected temperature of 190 °C could be reached within ca. 3 min upon microwave heating (Figure 1, profile b). These results clearly demonstrate that even small amounts of an ionic liquid are able to change the dielectric properties of an otherwise less polar solvent sufficiently so that more rapid heating to higher reaction temperatures becomes possible. Increasing the amount of bmimPF_6 to 0.075 mmol led, as expected, to a more rapid heating of the reaction mixture (Figure 1, profile c). Further doubling of the ionic liquid concentration to 0.150 mmol provided a profile that allowed heating of the bmimPF_6-doped DCE to 190 °C within ca. 1 min (Figure 1, profile d). These "microwave flash heating" conditions[11] could only be marginally improved by further increasing the ionic liquid concentration (profile e). To minimize the risk of potential contaminations or side reactions caused by the ionic liquid,[9] all the following cycloaddition studies were carried out using this set of conditions (0.150 mmol bmimPF_6 for 2 mL of DCE, profile d). Indeed, under these conditions the intramolecular hetero-Diels−Alder reaction **1a** → **3a** (including the hydrolysis **2a** → **3a**, see below) was completed in only 18 min For the other three examples, similar fast transformations could be achieved (see Scheme 1). For the hetero-Diels−Alder cycloaddition reactions described herein we ascribe the rate-enhancement on going from neat DCE (170 °C) to ionic liquid-doped DCE (190 °C) to the 20 °C higher reaction temperature, not to any specific effect caused by the ionic liquid. This assumption was supported by a control experiment where the cycloaddition/hydrolysis **1a** → **3a** was performed with the 0.150 mmol bmimPF_6/DCE mixture at 170 °C. Indeed the reaction time needed for complete conversion (ca. 40 min) was more or less identical to the experiment performed in neat DCE described above. Evidently, the concentration or type of ionic liquid used in our studies is not suitable for influencing the particular Diels−Alder chemistry directly.[12]

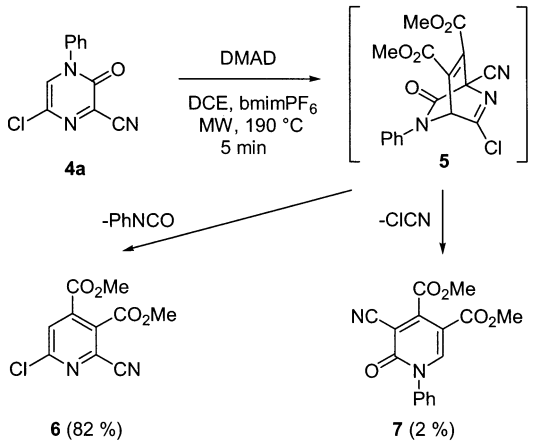
The initial products of the intramolecular Diels−Alder reactions displayed in Scheme 1 are the "imidoyl chloride" polycycles **2**.[4] In general, these products are moisture sensitive and hydrolyze to the more stable "bislactams" **3** either spontaneously (for **2a**), or by stirring in chloroform in the open atmosphere for 18 h.[4] We discovered that rapid hydrolysis of the intermediates **2b**−**d** could be achieved by addition of water (80 μL) through the septum of the microwave process vial and resubjection of the reaction mixture to microwave irradiation (130 °C, 5 min). The isolated overall yields of **3a**−**d** after silica gel chromatography were 57−77% (Scheme 1).[16] These yields are in the same range as reported for the conven-

(13) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. *Chem. Soc. Rev.* **1998**, *27*, 213−223.

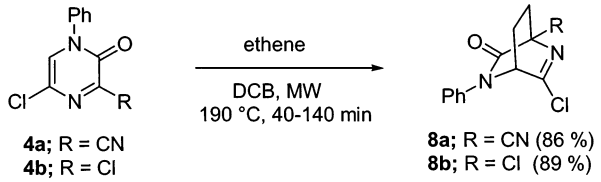
(14) For a detailed description of the single-mode microwave reactor, see the following: Stadler, A.; Kappe, C. O. *J. Comb. Chem.* **2001**, *3*, 624−630.

(15) For a discussion of the concept of molecular radiators, see, for example: (a) Kaiser, N.-F.; Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3595−3598. (b) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199−9223.

SCHEME 2



SCHEME 3



tional thermal protocols (60−74%).[4] However, the microwave-promoted transformations described herein now allow a more rapid and efficient one-pot access to cycloadducts of type **3**, that form the structural core of the natural product brevianamide (n = 2).[4] Note that the overall reaction times for the two-step process **1** → **2** → **3** were reduced from 2 to 3 days under conventional conditions, to 13−20 min under microwave/ionic liquid conditions.

We next turned our attention to cycloaddition reactions of 2(1*H*)-pyrazinones with acetylenic dienophiles. These Diels−Alder reactions generally lead to mixtures of pyridine and pyridone products via two competing spontaneous retro-Diels−Alder fragmentation pathways from the initially formed bicyclic cycloadducts (Scheme 2).[17] Employing the 2(1*H*)-pyrazinone precursor **4a** as model substrate we have studied the cycloaddition reaction with dimethylacetylenedicarboxylate (DMAD) under the microwave/ionic liquid conditions used above (190 °C, DCE/bmimPF_6). Utilizing the microwave protocol (10 equiv of DMAD), pyridine **6** and pyridone **7** were obtained in 82% and 2% isolated yield, respectively, after only 5 min of microwave irradiation.[16] These results are consistent in terms of product yields and ratios, with the data obtained under thermal conditions where DMAD was utilized as the solvent under reflux conditions (140 °C, 30 min).[17]

The third cycloaddition route investigated in the 2(1*H*)-pyrazinone series involved the Diels−Alder cycloaddition reaction of the heterocyclic pyrazinone heterodienes **4a**,**b** with ethene, leading to the bicyclic cycloadducts **8a**,**b** (Scheme 3). Under conventional conditions, these cycloaddition reactions have to be carried out in an autoclave applying 25 atm ethene pressure before the setup is heated to 110 °C for 12 h.[18] We were particularly interested to see how the high-temperature microwave protocol would compare with the elevated pressure conditions.[19]

Our initial experiments in this series utilized again the optimized bmimPF_6/DCE conditions (Figure 1, profile d). Since the microwave reactor setup used in the current study[14] would not allow pre-pressurization of the reaction vessel with ethene, we saturated the solution of 2-(1*H*)-pyrazinone **4a** contained in the microwave process vial with gaseous ethene at atmospheric pressure, before sealing the vial with the standard aluminum/Teflon crimp.[14] Interestingly, microwave irradiation of this mixture at 190 °C led to a spontaneous decomposition/runaway reaction that caused precipitation of an insoluble material on the glass wall of the microwave vial.[20]

Therefore, we changed to conditions where the ionic liquid was eliminated from the protocol. As a suitable solvent we have chosen the strongly microwave absorbing 1,2-dichlorobenzene (DCB),[21] allowing us to carry out the cycloaddition chemistry in the range of 180−250 °C utilizing microwave flash heating. For pyrazinone precursor **4a**, Diels−Alder addition of ethene in the sealed microwave vial was completed after irradiation for 40 min at 190 °C leading to an isolated yield of 86% of pure cycloadduct (82% under conventional thermal conditions).[18] Interestingly, it was not possible to further increase the reaction rate by raising the temperature. At temperatures above 200 °C an equilibrium between the cycloaddition **4a** → **8a** and the competing retro-Diels−Alder fragmentation process was observed. This was confirmed by subjecting a sample of cycloadduct **8a** to microwave heating (without ethene) in DCB at 250 °C, leading to a mixture of the 2(1*H*)-pyrazinone precursor **4a** and the cycloadduct **8a** in a ratio of ca. 1:3. For 2(1*H*)-pyrazinone derivative **4b** an irradiation time of 140 min at 190 °C was required to carry the cycloaddition to completion (89% isolated yield), in agreement with the known decreased reactivity of this heterodiene (86% isolated yield of **4b** under conventional conditions).[18] To perform microwave-assisted protocols utilizing gaseous reagents as described herein, it would clearly be desirable to have a setup where a microwave compatible small-scale reaction vessel could be pressurized with a gaseous reagent before irradiating with microwaves. On the other hand, note that the present microwave-assisted cycload-

(16) All products were indentified and characterized on the basis of their ^{1}H NMR spectrum and comparison with authentic materials.

(17) Tutonda, M., Vanderzande, D., Hendrickx, M., Hoornaert, G. *Tetrahedron* **1990**, *46*, 5715−5732.

(18) Loosen, K. P.; Tutonda, M. G.; Khorasani, M. F.; Compernolle, F.; Hoornaert, G. J. *Tetrahedron* **1991**, *47*, 9259−9268.

(19) For the use of gaseous reagents in microwave-assisted processes, see, for example: Tanner, D. D.; Kandanarachchi, P.; Ding, Q.; Shao, H.; Vizitiu, D.; Franz, J. A. *Energy Fuels* **2001**, *15*, 197−204.

(20) ***CAUTION!*** This precipitate resulted in extreme microwave absorption accompanied by a rapid increase in pressure that resulted in an automatic shut-down of the microwave reactor, and caused thermal cracks to appear on the glass vial. We assume that an ionic liquid-initiated polymerization of ethene had occurred, that caused precipitation of strongly microwave absorbing ionic liquid-doped polyethylene on the glass vial. In the absence of the ionic liquid a normal heating pattern was observed. For examples of ionic liquid-initiated polymerizations of olefins, see, the following: (a) Hong, K.; Zhang, H.; Mays, J. W.; Visser, A. E.; Brazel, C. S.; Holbrey, J. D.; Reichert, W. M.; Rogers, R. D. *Chem. Commun.* **2002**, 1368−1369. (b) Zhang, H.; Hong, K.; Mays, J. W. *Macromolecules* **2002**, *35*, 5738−5741. (c) Hlatky, G. G Patent WO 0181436, 2001.

(21) (a) Bose, A. K.; Banik, B. K.; Lavlinskaia, N.; Jayaraman, M.; Manhas, M. S. *Chemtech* **1997**, *27*, 18−24. (b) Strohmeier, G. A.; Kappe, C. O. *J. Comb. Chem.* **2002**, *4*, 154−161.

ditions do not require a significant ethene pressure (measured total pressure in the microwave vial at 190 °C 1−2 bar), but are nevertheless significantly faster than the earlier published autoclave methods (25 atm ethene pressure at 110 °C for 12 h (**4a**) and 16 h (**4b**)). We believe that this is a consequence of the higher reaction temperatures utilized in the microwave protocol, compensating for the lower pressure.

In conclusion, we have demonstrated that inter- and intramolecular hetero-Diels−Alder reactions of functionalized 2(1*H*)-pyrazinones can be carried out rapidly utilizing microwave flash heating. For these transformations, low-boiling solvents such as 1,2-dichloroethane, doped with small amounts of an ionic liquid are generally ideal reaction media as they allow very rapid heating by microwaves in sealed vessels in combination with a facilitated reaction workup. In addition, we have shown that the use of a gaseous reagent in a sealed vessel microwave experiment may provide an alternative, more efficient method to carry out synthetic transformations in comparison to standard autoclave protocols. Significant rate-enhancements for both inter- and intramolecular hetero-Diels−Alder reactions were observed comparing the standard protocols to the microwave-heated transformations. In all the investigated Diels−Alder additions, yields and product distributions were very similar to what has been observed under conventional thermal conditions.

Experimental Section

General Methods. For a general description of methods and microwave irradiation procedures, see ref 14. All cycloaddition products have previously been characterized, and the data obtained corresponded satisfactorily with NMR and MS data, and comparison with authentic samples.

General Procedure for the Synthesis of Cycloadducts 3a−d. A solution of the corresponding 3-alkenyl(oxy)-2(1*H*)-pyrazinone **1b**−**d**[4] (100 mg) and bmimPF_6 (30 μL, 0.15 mmol) in 1,2-dichloroethane (2 mL; freshly distilled) is irradiated at 190 °C preselected maximum temperature (see Scheme 1 for irradiation times). Experiments were carried out in a 5 mL sealed microwave process vial. Then water (80 μL) is added through the septum of the microwave process vial and the reaction mixture is heated at 130 °C preselected maximum temperature for an additional 5 min. The reaction was worked up by diluting the mixture with CH_2Cl_2. The mixture was subsequently washed with a saturated solution of $NaHCO_3$ and brine and the organic layer was dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent the crude product was purified by column chromatography over silica gel using ethyl acetate as the eluent. For compound **1a**, it is not necessary to add water as spontaneous hydrolysis of **2a** occurs during reaction. All compounds were identified on the basis of their NMR and MS spectra and comparison with authentic materials. For spectral data of compounds synthesized under conventional heating conditions, see ref 4.

Data for 3a: yield 74%; mp 141−142 °C (lit.[4] mp 142 °C); IR (KBr) 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.23 (m, 5H), 6.68 (br s, 1H), 4.92 (d, J = 15 Hz, 1H), 4.38 (ddd, J = 9, 8, 1 Hz, 1H), 4.30 (ddd, J = 10, 8, 6 Hz, 1H), 4.27 (d, J = 15.0 Hz, 1H), 3.88 (ddd, J = 5, 2, 1 Hz, 1H), 2.48−2.35 (m, 1H), 2.30−2.24 (m, 1H), 1.89 (m, 2H), 1.55 (ddd, J = 14, 7, 1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5, 168.7, 136.1, 128.9, 128.1, 128.0, 91.4, 73.0, 60.1, 48.3, 43.3, 28.5, 26.1; CIMS m/z 273 (MH^+).

Data for 3b: yield 67%; mp 255 °C (lit.[4] mp 254 °C); IR (KBr) 1704 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46−7.22 (m, 5H), 6.21 (br s, 1H), 4.50−4.29 (m, 3H), 2.73−2.48 (m, 2H), 2.38 (br quintuplet(dddd), J = 6 Hz, 1H), 2.03 (br quintuplet (dddd), J = 6 Hz, 1H), 1.87 (dd, J = 14, 6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.0, 167.3, 138.9, 129.3, 126.8, 124.3, 91.4, 73.3, 63.7, 42.8, 28.6, 26.2; EIMS m/z 258 (M^+, 4), 137 (M^+ − PhNHCHO, 100).

Data for 3c: yield 57%; IR (KBr) 1698 cm^{-1}; 1H NMR ($CDCl_3$, 400 MHz) δ 7.32−7.21 (m, 5H), 6.73 (br s, 1H), 4.87 (d, J = 14 Hz, 1H), 4.33 (d, J = 14 Hz, 1H), 4.14−4.10 (m, 1H), 3.80−3.73 (m, 2H), 2.04−1.87 (m, 3H), 1.86−1.74 (m, 1H), 1.67−1.49 (m, 2H), 1.24 (dbrd, J = 12, 5 Hz, (<1 Hz), 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 168.5, 136.0, 128.9, 128.2, 128.1, 83.5, 67.1, 58.3, 48.6, 35.6, 30.3, 25.6, 24.0; CIMS m/z 287 (MH^+).

Data for 3d: yield 77%; IR (KBr) 1710, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.22 (m, 5H), 7.09 (s, 1H), 4.38−4.35 (m, 1H), 4.13 (ddd, J = 10, 2, 1 Hz, 1H), 3.97 (ddd, J = 10, 10, 1 Hz, 1H), 2.52 (ddd, J = 13, 10, 5 Hz, 1H), 2.26−2.16 (m, 1H), 2.07−1.99 (m, 1H), 1.89−1.76 (m, 1H), 1.72−1.60 (m, 2H), 1.54 (ddd, J = 13, 5, 1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 167.3, 139.8, 129.2, 127.3, 124.8, 84.5, 64.0, 62.3, 35.1, 30.9, 26.6, 25.5; EIMS m/z 272 (M^+, 10), 153 (M^+ − PhNCO, 100), 151 (M^+ − PhNHCHO, 70); HRMS exact mass for $C_{15}H_{16}N_2O_3$ 272.1161, found 272.1162.

Procedure for the Synthesis of Compounds 6 and 7. A solution of the 3-cyano-2(1*H*)-pyrazinone **4a**[17] (100 mg), bmimPF_6 (15 μL), and dimethyl acetylenedicarboxylate (532 μL) in 1,2-dichloroethane (1 mL; freshly distilled) is irradiated for 5 min at 190 °C preselected maximum temperature. Experiments were carried out in a 2 mL sealed microwave process vial. The reaction was worked up by diluting the mixture with CH_2Cl_2. The mixture was subsequently washed with a saturated solution of $NaHCO_3$ and brine, and the organic layer was dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the crude products **6** and **7** were purified by column chromatography over silica gel using a gradient elution selecting different mixtures of hexane/ethyl acetate as the eluent ranging from 100% hexane-to-a ratio of 6:4. Both compounds were identified on the basis of their NMR spectra and comparison with authentic materials. For spectral data of compounds synthesized under conventional heating conditions, see ref 17.

Data for 6: yield 82%; mp 92−93 °C (lit.[17] mp 93 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 4.03 (s, 3H), 3.91 (s, 3H); EIMS m/z 254 (M^+, 14), 222 (100).

Data for 7: yield 2%; mp 158 °C (lit.[17] mp 158 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.41 (s, 1H); 7.38 (m, 5H), 4.01 (s, 3H), 3.80 (s, 3H); EIMS m/z 312 (M^+, 96), 281 (52), 253 (100).

Procedure for the Synthesis of Cycloadducts 8a,b. A solution of the corresponding 2(1*H*)-pyrazinone **4a**,**b**[5] (50 mg) in 1,2-dichlorobenzene (5 mL) is saturated with ethene by passing the gas through the solution for 30 min at atmospheric pressure. The solution is irradiated at 190 °C preselected maximum temperature (see body text for irradiation times). Experiments were carried out in a 5 mL sealed microwave process vial. The reaction was worked up by evaporating the 1,2-dichlorobenzene. The crude product was purified by column chromatography over silica gel using a gradient elution selecting different mixtures of hexane/ethyl acetate as the eluent ranging from 100% hexane-to-a ratio of 6:4. Both compounds were identified on the basis of their NMR spectra and comparison with authentic materials. For spectral data of compounds synthesized under conventional heating conditions, see ref 5. In case of the imidoyl chloride **8b**, hydrolysis to the corresponding bislactam occurred during chromatography.

Data for 8a: Yield 86%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.22 (m, 5H), 4.93 (dd, 1H), 2.72−2.05 (m, 4H); EIMS m/z 259 (M^+, 3), 119 ($PhNCO^+$, 100).

Data for 8b: yield 89%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54−7.25 (m, 5H), 4.97 (m, 1H), 2.52−1.94 (m, 4H); EIMS m/z 268 (M^+, 5), 149 (M^+ − PhNCO, 87), 119 ($PhNCO^+$, 100).

Acknowledgment. We thank PersonalChemistry AB (Uppsala, Sweden) for the use of the SmithSynthesizer. We are also grateful to the Research Fund Katholieke Universiteit Leuven for financial support.

JO0263216