Ring-Closing Metathesis Approach to 2*H*-2-Benzazepine-1,3-diones

Stéphane Lebrun,[a,b] Axel Couture,*[a,c] Eric Deniau,[a,b] Pierre Grandclaudon[a,b]

[a] Université Lille Nord de France, 59000 Lille, France
Fax +33(3)20436309; E-mail: axel.couture@univ-lille1.fr

[b] USTL, Laboratoire de Chimie Organique Physique, EA CMF 4478, Bâtiment C3(2), 59655 Villeneuve d'Ascq Cedex, France

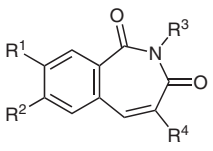
[c] CNRS, UMR 8181 'UCCS', Bâtiment C3(2), 59655 Villeneuve d'Ascq Cedex, France

Received 1 December 2010; revised 9 December 2010

Abstract: A series of diversely substituted 2*H*-2-benzazepine-1,3-diones were efficiently prepared from the unsaturated precursors, *N*-acyl-*o*-vinylbenzamides, through a ring-closing metathesis reaction. The parent compounds were easily obtained from the appropriate *o*-vinylbenzoic acids.

Key words: fused-ring systems, acylation, ring closure, metathesis, imides

Benzo-fused heterocyclic ring systems have received a lot of attention over the years because of their ubiquitous appearance in natural products and modern pharmaceuticals.[1] 2-Benzazepines and their oxo derivatives at different oxidation levels fall into this category. They are a class of benzo-fused nitrogen-containing seven-membered heterocyclic rings, which are important structural features of marketed drugs, clinical candidates, and other bioactive molecules.[2] As a consequence, the development of synthetic methodologies that may have generality for the construction of multifarious substituted and unsubstituted benzazepines is an area of current interest and alternative methods are currently the object of synthetic endeavor. In this context we envisioned the assembly of the corresponding α,β-unsaturated oxobenzolactams, that is, the 2*H*-2-benzazepine-1,3-diones **1a–f** (Figure 1). It was anticipated that these highly functionalized models could serve a key role as advanced intermediates prior to the conversion to tailor-made environmentally different benzazepine derivatives as they possess the requisite structure and functional groups location to be easily converted into seven-membered azaheterocyclic models. We surmised that ensuing rather simple chemical manipulation of the latent functionalities would allow for rapid achievement of molecular complexity in a highly efficient manner. Noteworthy compounds of this class are endowed with interesting chemotherapeutic properties. They have indeed been found to be CNS stimulants, in vitro antimicrobial agents and to induce motor activity.[3] They are also known to display potent inhibitory activity against cyclic adenosine phosphodiesterase and to act as sunscreen agents.[4] In contrast, the use of benzazepines with an unsaturation in the heterocyclic ring has seen very little synthetic application,[5] probably due to the lack of general synthetic methods for their elaboration. To the best of our knowledge, compounds structurally related to **1a–f** have only been obtained by N-alkylation of the corresponding NH-free models derived from PPA-induced annulation of *cis*-cinnamonitrile-*o*-carboxylic acid derivatives.[6] The latter compounds have been prepared by inverse Beckmann rearrangement of β-nitroso-α-naphthols.[7] This ring-expansion methodology is fraught with difficulties associated with the use of hazardous reagents and its applicability is unsatisfactory mainly because of restrictions in the choice of substituents on the aromatic unit and the seven-membered ring system as well. Additionally the *N*-phenyl derivative of a bare model has been incidentally obtained through condensation of triphenyl(phenyliminovinylidene)phosphorane with phthalaldehydic acid.[8]



1	R^1	R^2	R^3	R^4
a	H	H	Me	H
b	H	H	Pr	H
c	H	H	Bn	H
d	MeO	MeO	Me	H
e	OCH_2O		Me	H
f	OCH_2O		Me	Me

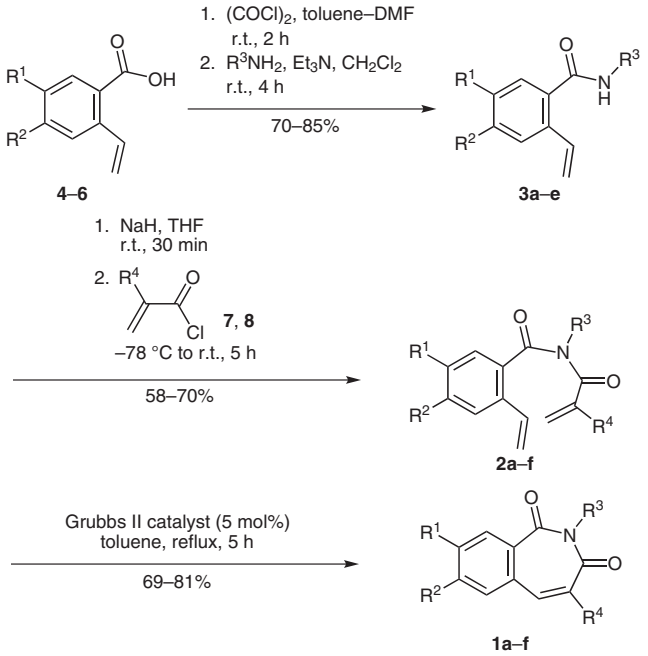
Figure 1 Targeted 2*H*-2-benzazepine-1,3-diones **1a–f**

Herein we wish to report a conceptually new synthetic approach to a variety of 2*H*-2-benzazepine-1,3-diones **1a–f** based upon the ultimate creation of the alkene moiety embedded in the azaheterocyclic unit on reliance with the ring-closing metathesis (RCM) strategy. Olefin RCM reaction has become a powerful tool in organic synthesis over the past decades, especially when well-characterized ruthenium catalysts were employed.[9] RCM reaction, which ranks high in the hierarchy of synthetic approaches for the elaboration of small, medium, and large unsaturated heterocycles, is now routinely applied to ensure the assembly of cyclic olefins of virtually all ring sizes containing ether, ester, amide, amine, and other functionalities.[10] However as far as we know, this annulation technique has not been applied to *N*-acylamide derivatives.

One way of constructing the targeted compounds **1a–f** would be by cyclization of the polyenic diacylamines **2a–f** as suitable precursors for the planned RCM reaction. The assembly of these highly functionalized opened models was envisioned and the first facet of the synthesis was the elaboration of the NH-free amides **3a–e**, which were

SYNTHESIS 2011, No. 4, pp 0669–0673
Advanced online publication: 19.01.2011
DOI: 10.1055/s-0030-1258416; Art ID: Z30110SS

readily obtained under standard conditions from the corresponding benzoic acids **4–6** (Scheme 1, Table 1). Deprotonation of **3a–e** with sodium hydride and subsequent interception of the transient sodium amide salt with a suitably (un)substituted acryloyl chloride **7**, **8** delivered quite satisfactory yields of the unsaturated *N*-acyl-*o*-vinylbenzamides **2a–f** (Scheme 1, Table 1).



Scheme 1 Synthesis of titled 2*H*-2-benzazepine-1,3-diones **1a–f**

The targeted imides **1a–f** were only one reaction away from the precursors **2a–f**. Thus, the ring-closing metathesis experiments was undertaken next and for this purpose the first- and second-generation Grubbs catalysts **9** and **10** were screened (Figure 2). At first, the seven-membered ring precursor **2a** underwent ring closure after heating under reflux in CH_2Cl_2 for 24 hours using 5 mol% first-generation Grubbs catalyst (**9**; reaction monitored by TLC); however, the benzazepinedione **1a** was isolated only in a moderate yield (32%). Increasing the amount of the same catalyst to 10 mol% had no significant impact on the process efficiency (35% vs. 32% yield for **1a**). However, it was pleasing to observe that the yield could be increased to 75% when the N-acylated *o*-vinylbenzamide **2a** was subjected to 5 mol% of the thermally more stable second-generation Grubbs catalyst (**10**) under reflux in toluene, which turned out to be the best solvent. These optimal conditions were then used to perform the annulation reaction of the structurally diverse styrene precursors **2b–f**. A representative series of compounds, which have been prepared by this technique are presented in Table 1, where it can be seen that this simple procedure affords very satisfactory yields of the targeted 2*H*-2-benzazepine-1,3-diones **1a–f**. The method tolerates the presence of diverse substituents on the aromatic unit and on the diacylated nitrogen atom as well. In strong contrast with the sole reported method for the synthesis of such compounds incorporation of substituents on the alkene moiety could also be envisaged owing to the availability of appropriate acryloyl chlorides, as exemplified by the efficient formation of the substituted model **1f** by RCM reaction applied to **2f**.

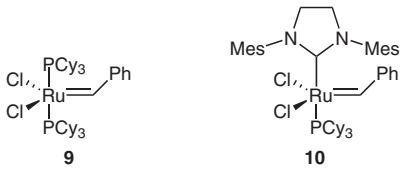


Figure 2 Common ruthenium catalysts used in RCM reactions

In summary, we have devised a short and efficient synthetic strategy towards a variety of hitherto hardly accessible 2*H*-2-benzazepine-1,3-diones. The key step of the synthetic sequence is based upon the creation of the alkene moiety present in the azepinedione template in the ultimate step via unprecedented RCM reaction.

This technique gives rise to a number of α,β-unsaturated oxolactam-type models, which can be regarded as versatile building blocks with the capacity to incorporate additional substituents/functionalities at a later stage. Applications of this strategy to highly substituted benzazepines synthesis are underway and will be reported in due course.

Table 1 Compounds **3a–e**, **2a–f** and **1a–f** Prepared

	NH-Free *o*-vinylbenzamide **3**				Acryloyl chloride **7**, **8**		*N*-Acyl-*o*-vinylbenzamide **2**		2*H*-2-Benzazepine-1,3-dione **1**	
	R^1	R^2	R^3	Yield (%)		R^4		Yield (%)		Yield (%)
3a	H	H	Me	70	**7**	H	**2a**	70	**1a**	75
3b	H	H	Pr	76	**7**	H	**2b**	66	**1b**	69
3c	H	H	Bn	85	**7**	H	**2c**	60	**1c**	81
3d	OMe	OMe	Me	75	**7**	H	**2d**	63	**1d**	72
3e	OCH_2O		Me	82	**7**	H	**2e**	65	**1e**	78
3e	OCH_2O		Me	–	**8**	Me	**2f**	58	**1f**	70

All solvents were dried and distilled according to standard procedures. Dry glassware was obtained by oven-drying and assembling under dry argon. The glassware was equipped with rubber septa and reagent transfer was performed by syringe techniques. For flash chromatography, Merck silica gel 60 (40–63 μm, 230–400 mesh ASTM) was used. The melting points were obtained on a Reichert-Thermopan apparatus and are not corrected. Elemental analyses were obtained using a Carlo-Erba CHNS-11110 equipment. NMR spectra were recorded on a Bruker AM 300 spectrometer (300 MHz and 75 MHz, for ^{1}H, and ^{13}C) with $CDCl_3$ as solvent and Me_4Si as internal standard.

The *o*-vinylbenzoic acids **4**,[11] **5**,[12] **6**[12] were prepared following literature procedures.

4,5-Dimethoxy-2-vinylbenzoic Acid (5)
Mp 183–185 °C (Lit.[13] mp 183–184 °C).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.94 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 5.32 (d, *J* = 10.9 Hz, 1 H_{vinyl}), 5.59 (d, *J* = 17.4 Hz, 1 H_{vinyl}), 7.05 (s, 1 H_{arom}), 7.57 (s, 1 H_{arom}), 7.64 (dd, *J* = 10.9, 17.4 Hz, 1 H_{vinyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.0 (2 × OCH_3), 109.6 (CH_2), 113.4 (CH), 115.4 (CH), 119.2 (C), 135.6 (C), 136.2 (CH), 148.0 (C), 152.7 (C), 172.4 (C=O).

6-Vinylbenzo[1,3]dioxole-5-carboxylic Acid (6)
Mp 165–167 °C (Lit.[12] mp 163–164 °C).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 5.22 (d, *J* = 11.0 Hz, 1 H_{vinyl}), 5.65 (d, *J* = 17.5 Hz, 1 H_{vinyl}), 6.10 (s, 2 H, OCH_2O), 7.20 (s, 1 H_{arom}), 7.28 (s, 1 H_{arom}), 7.46 (dd, *J* = 11.0, 17.5 Hz, 1 H_{vinyl}), 12.85 (br s, 1 H, CO_2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 101.9 (OCH_2O), 105.8 (CH), 109.3 (CH), 115.2 (CH_2), 123.0 (C), 134.5 (C), 134.9 (CH), 146.7 (C), 150.4 (C), 167.6 (C=O).

NH-Free *o*-Vinybenzamides 3a–e; General Procedure
A mixture of benzoic acid derivative **4**–**6** (20 mmol), oxalyl chloride (50 mmol), and DMF (0.5 mL) in freshly distilled toluene (40 mL) was stirred for 2 h at r.t.. The solvent was removed under vacuum and the residue was dissolved in CH_2Cl_2 (10 mL). The solution was added dropwise to a solution of amine R^3NH_2 (20 mmol) and Et_3N (40 mmol) in CH_2Cl_2 (30 mL) at 0 °C, then the mixture was stirred at r.t. for 4 h. H_2O (30 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under vacuum. Benzamides **3a**–**e** were purified by flash column chromatography on silica gel using EtOAc–hexanes (80:20) as eluent and finally recrystallized from hexane–toluene (Tables 1 and 2).

***N*-Eneacyl-*o*-vinylbenzamides 2a–f; General Procedure**
A solution of benzamide **3a**–**e** (4.5 mmol) in anhyd THF (5 mL) was added dropwise to a suspension of NaH (5.4 mmol) in anhyd THF (20 mL) at 0 °C. The reaction mixture was stirred for 30 min at r.t. and cooled to –78 °C. The appropriate acryloyl chloride **7**, **8** (9 mmol) was then added dropwise. After stirring for 5 min at –78 °C, the mixture was allowed to warm to r.t. over 5 h. H_2O (10 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 30 mL). The combined extracts were dried ($MgSO_4$) and the solvent was removed under vacuum. The residue was purified by flash column chromatography on silica gel using EtOAc–hexanes (10:90) as eluent to afford *N*-acylamides **2a**–**f** as yellow oils (Tables 1 and 2).

2*H*-2-Benzazepine-1,3-diones 1a–f; General Procedure
A solution of *N*-acylamide **2a**–**f** (1.5 mmol) and second-generation Grubbs catalyst (0.075 mmol, 5 mol%) in anhyd toluene (20 mL) was refluxed under stirring for 5 h under argon (monitored by TLC to establish completion of the reaction). The reaction mixture was concentrated under vacuum and the resulting residue was purified by flash column chromatography on silica gel using EtOAc–hexanes (30:70) as eluent to furnish 2*H*-2-benzazepine-1,3-diones **1a**–**f** as yellow oils (Tables 1 and 2).

Table 2 Physical and Spectroscopic Data of Carboxamides **3a**–**e**, *N*-Eneacylamides **2a**–**f**, and Benzazepinediones **1a**–**f** Prepared

Product[a]	Mp (°C)	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
3a	125–127 (123–124)[14]	2.98 (d, *J* = 5.0 Hz, 3 H, NCH_3), 5.34 (dd, *J* = 1.0, 11.0 Hz, 1 H_{vinyl}), 5.71 (dd, *J* = 1.0, 17.5 Hz, 1 H_{vinyl}), 5.85 (br s, 1 H, NH), 7.02 (dd, *J* = 11.0, 17.5 Hz, 1 H_{vinyl}), 7.24–7.31 (m, 1 H_{arom}), 7.35–7.44 (m, 2 H_{arom}), 7.56 (d, *J* = 7.7 Hz, 1 H_{arom})	26.8 (NCH_3), 116.7 (CH_2), 126.2 (CH), 127.4 (CH), 127.7 (CH), 130.1 (CH), 134.5 (CH), 135.7 (C), 150.6 (C), 171.5 (C=O)
3b	62–64 (62–63)[14]	0.97 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.62 (quint, *J* = 7.4 Hz, 2 H), 3.38 (m, 2 H, NCH_2), 5.33 (d, *J* = 10.9 Hz, 1 H_{vinyl}), 5.69 (d, *J* = 17.4 Hz, 1 H_{vinyl}), 5.98 (br s, 1 H, NH), 7.04 (dd, *J* = 10.9, 17.5 Hz, 1 H_{vinyl}), 7.21–7.28 (m, 1 H_{arom}), 7.34–7.45 (m, 2 H_{arom}), 7.56 (d, *J* = 7.8 Hz, 1 H_{arom})	11.5 (CH_3), 22.8 (CH_2), 41.7 (NCH_2), 116.6 (CH_2), 126.1 (CH), 127.4 (CH), 127.7 (CH), 130.0 (CH), 134.5 (CH), 135.6 (C), 135.7 (C), 169.4 (C=O)
3c	88–90 (88–89)[14]	4.58 (d, *J* = 5.8 Hz, 2 H, NCH_2), 5.12 (d, *J* = 11.0 Hz, 1 H_{vinyl}), 5.71 (d, *J* = 17.5 Hz, 1 H_{vinyl}), 6.55 (br s, 1 H, NH), 7.06 (dd, *J* = 11.0, 17.5 Hz, 1 H_{vinyl}), 7.25–7.53 (m, 8 H_{arom}), 7.82 (d, *J* = 7.6 Hz, 1 H_{arom})	43.9 (NCH_2), 116.6 (CH_2), 126.1 (CH), 127.4 (CH), 127.6 (CH), 128.0 (2 × CH), 128.3 (2 × CH), 130.1 (CH), 131.9 (CH), 134.5 (CH), 135.4 (C), 137.4 (C), 138.3 (C), 169.5 (C=O)
3d	140–142 (colorless crystals)	2.96 (d, *J* = 4.8 Hz, 3 H, NCH_3), 3.87 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 5.28 (d, *J* = 10.9 Hz, 1 H_{vinyl}), 5.59 (d, *J* = 17.4 Hz, 1 H_{vinyl}), 6.02 (br s, 1 H, NH), 6.97 (s, 1 H_{arom}), 7.00 (s, 1 H_{arom}), 7.02 (dd, *J* = 10.9, 17.4 Hz, 1 H_{vinyl})	26.8 (NCH_3), 55.9 (OCH_3), 56.0 (OCH_3), 108.5 (CH_2), 110.5 (CH), 115.2 (CH), 127.9 (C), 129.0 (C), 134.5 (CH), 140.4 (C), 150.2 (C), 169.6 (C=O)
3e	136–138 (colorless crystals)	2.93 (d, *J* = 4.8 Hz, 3 H, NCH_3), 5.23 (dd, *J* = 0.9, 10.9 Hz, 1 H_{vinyl}), 5.54 (dd, *J* = 0.9, 17.9 Hz, 1 H_{vinyl}), 5.92 (s, 2 H, OCH_2O), 6.03 (br s, 1 H, NH), 6.86 (s, 1 H_{arom}), 6.89 (dd, *J* = 10.9, 17.4 Hz, 1 H_{vinyl}), 6.97 (s, 1 H_{arom})	26.8 (NCH_3), 101.6 (OCH_2O), 105.7 (CH), 107.5 (CH), 115.0 (CH_2), 129.6 (C), 130.8 (C), 134.1 (CH), 147.1 (C), 149.1 (C), 169.4 (C=O)

Table 2 Physical and Spectroscopic Data of Carboxamides **3a–e**, *N*-Eneacylamides **2a–f**, and Benzazepinediones **1a–f** Prepared (continued)

Product[a]	Mp (°C)	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ
2a	oil	3.21 (s, 3 H, NCH_3), 5.39 (dd, *J* = 0.9, 11.0 Hz, 1 H_{vinyl}), 5.56 (dd, *J* = 1.8, 10.1 Hz, 1 H_{vinyl}), 5.74 (dd, *J* = 0.9, 17.3 Hz, 1 H_{vinyl}), 6.27 (dd, *J* = 1.8, 16.8 Hz, 1 H_{vinyl}), 6.46 (dd, *J* = 10.1, 16.8 Hz, 1 H_{vinyl}), 6.83 (dd, *J* = 11.0, 17.3 Hz, 1 H_{vinyl}), 7.24–7.32 (m, 2 H_{arom}), 7.42–7.49 (m, 1 H_{arom}), 7.58 (d, *J* = 7.9 Hz, 1 H_{arom})	32.8 (NCH_3), 118.0 (CH_2), 126.3 (CH), 127.6 (CH), 128.0 (CH), 128.7 (CH_2), 130.6 (CH), 131.0 (CH), 133.1 (CH), 134.9 (C), 135.9 (C), 169.2 (C=O), 172.9 (C=O)
2b	oil	0.88 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.64 (quint, *J* = 7.4 Hz, 2 H), 3.70–3.75 (m, 2 H, NCH_2), 5.41 (dd, *J* = 0.9, 11.0 Hz, 1 H_{vinyl}), 5.45–5.50 (m, 1 H_{vinyl}), 5.73 (dd, *J* = 0.9, 17.4 Hz, 1 H_{vinyl}), 6.15–6.27 (m, 2 H_{vinyl}), 6.88 (dd, *J* = 11.0, 17.4 Hz, 1 H_{vinyl}), 7.25–7.29 (m, 2 H_{arom}), 7.41–7.47 (m, 1 H_{arom}), 7.59 (d, *J* = 7.9 Hz, 1 H_{arom})	11.4 (CH_3), 22.1 (CH_2), 47.3 (NCH_2), 117.8 (CH_2), 126.2 (CH), 127.7 (CH), 127.8 (CH), 128.2 (CH_2), 130.9 (CH), 131.1 (CH), 133.2 (CH), 135.2 (C), 136.3 (C), 169.2 (C=O), 173.0 (C=O)
2c	oil	5.03 (s, 2 H, NCH_2), 5.32 (dd, *J* = 0.9, 10.9 Hz, 1 H_{vinyl}), 5.45 (dd, *J* = 5.0, 6.7 Hz, 1 H_{vinyl}), 5.70 (dd, *J* = 0.9, 17.4 Hz, 1 H_{vinyl}), 6.18–6.26 (m, 2 H_{vinyl}), 6.79 (dd, *J* = 10.9, 17.4 Hz, 1 H_{vinyl}), 7.25–7.58 (m, 9 H_{arom})	48.6 (NCH_2), 117.9 (CH_2), 126.3 (CH), 127.6 (CH), 127.7 (CH), 128.0 (CH), 128.4 (2 × CH), 128.5 (2 × CH), 128.7 (CH_2), 130.7 (CH), 131.3 (CH), 133.1 (CH), 134.9 (C), 136.6 (C), 137.1 (C), 169.3 (C=O), 172.9 (C=O)
2d	oil	3.21 (s, 3 H, NCH_3), 3.85 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 5.27 (d, *J* = 10.9 Hz, 1 H_{vinyl}), 5.48 (dd, *J* = 1.6, 9.7 Hz, 1 H_{vinyl}), 5.58 (d, *J* = 17.2 Hz, 1 H_{vinyl}), 6.22–6.31 (m, 2 H_{vinyl}), 6.75 (dd, *J* = 10.9, 17.2 Hz, 1 H_{vinyl}), 6.80 (s, 1 H_{arom}), 6.98 (s, 1 H_{arom})	32.8 (NCH_3), 56.0 (OCH_3), 56.1 (OCH_3), 108.3 (CH), 110.6 (CH), 116.3 (CH_2), 127.0 (C), 128.2 (CH_2), 130.3 (CH), 130.4 (C), 132.9 (CH), 148.8 (C), 151.3 (C), 169.2 (C=O), 172.8 (C=O)
2e	oil	3.23 (s, 3 H, NCH_3), 5.29 (d, *J* = 11.2 Hz, 1 H_{vinyl}), 5.56 (dd, *J* = 1.7, 10.1 Hz, 1 H_{vinyl}), 5.61 (d, *J* = 17.2 Hz, 1 H_{vinyl}), 6.05 (s, 2 H, OCH_2O), 6.24 (dd, *J* = 1.9, 16.8 Hz, 1 H_{vinyl}), 6.42 (dd, *J* = 10.1, 16.8 Hz, 1 H_{vinyl}), 6.75 (dd, *J* = 11.2, 17.2 Hz, 1 H_{vinyl}), 6.80 (s, 1 H_{arom}), 7.03 (s, 1 H_{arom})	32.9 (NCH_3), 101.9 (OCH_2O), 105.9 (CH), 107.7 (CH), 116.6 (CH_2), 128.5 (CH_2), 128.7 (C), 130.5 (CH), 132.0 (C), 132.7 (CH), 147.5 (C), 150.3 (C), 169.1 (C=O), 172.5 (C=O)
2f	oil	1.62 (s, 3 H, CH_3), 3.35 (s, 3 H, NCH_3), 5.13 (s, 1 H_{vinyl}), 5.21 (s, 1 H_{vinyl}), 5.28 (d, *J* = 10.9 Hz, 1 H_{vinyl}), 5.57 (d, *J* = 17.3 Hz, 1 H_{vinyl}), 6.01 (s, 2 H, OCH_2O), 6.67 (s, 1 H_{arom}), 6.76 (dd, *J* = 10.9, 17.3 Hz, 1 H_{vinyl}), 7.01 (s, 1 H_{arom})	18.3 (CH_3), 32.8 (NCH_3), 101.9 (OCH_2O), 105.9 (CH), 108.1 (CH), 116.3 (CH_2), 120.7 (CH_2), 127.5 (C), 132.5 (C), 133.3 (CH), 142.7 (C), 147.2 (C), 149.8 (C), 172.7 (C=O), 175.3 (C=O)
1a	oil	3.51 (s, 3 H, NCH_3), 6.47 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 7.07 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 7.42 (dd, *J* = 1.6, 7.3 Hz, 1 H_{arom}), 7.55–7.67 (m, 2 H_{arom}), 8.31 (dd, *J* = 1.7, 7.9 Hz, 1 H_{arom})	33.3 (NCH_3), 125.9 (CH), 130.7 (CH), 131.6 (CH), 132.1 (C), 132.7 (CH), 133.6 (CH), 137.5 (C), 138.3 (CH), 165.8 (C=O), 168.1 (C=O)
1b	oil	0.95 (t, *J* = 7.4, 3 H, CH_3), 1.69 (quint, *J* = 7.4, 2 H), 4.02–4.10 (m, 2 H, NCH_2), 6.42 (d, *J* = 12.4, 1 H_{vinyl}), 7.02 (d, *J* = 12.4, 1 H_{vinyl}), 7.38 (d, *J* = 7.3, 1 H_{arom}), 7.51–7.62 (m, 2 H_{arom}), 8.23 (d, *J* = 7.8, 1 H_{arom})	11.5 (CH_3), 21.2 (CH_2), 48.1 (NCH_2), 126.4 (CH), 130.5 (CH), 131.1 (CH), 132.1 (C), 132.5 (CH), 133.4 (CH), 133.5 (C), 137.7 (CH), 165.6 (C=O), 168.1 (C=O)
1c	oil	5.35 (s, 2 H, NCH_2), 6.48 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 7.06 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 7.21–7.33 (m, 3 H_{arom}), 7.38–7.45 (m, 3 H_{arom}), 7.53–7.66 (m, 2 H_{arom}), 8.24 (dd, *J* = 0.9, 7.6 Hz, 1 H_{arom})	49.2 (NCH_2), 126.2 (CH), 127.3 (CH), 128.3 (2 × CH), 128.4 (2 × CH), 130.7 (CH), 131.4 (CH), 132.2 (C), 132.8 (CH), 133.1 (C), 133.7 (CH), 137.4 (C), 138.2 (CH), 165.7 (C=O), 167.9 (C=O)
1d	oil	3.52 (s, 3 H, NCH_3), 3.98 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 6.40 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 6.81 (s, 1 H_{arom}), 6.97 (d, *J* = 12.4 Hz, 1 H_{vinyl}), 7.90 (s, 1 H_{arom})	33.3 (N CH_3), 56.2 (OCH_3), 56.3 (OCH_3), 113.3 (CH), 115.5 (CH), 124.2 (CH), 126.1 (C), 126.9 (C), 138.1 (CH), 150.6 (C), 152.2 (C), 165.8 (C=O), 166.7 (C=O)
1e	oil	3.51 (s, 3 H, NCH_3), 6.14 (s, 2 H, OCH_2O), 6.40 (d, *J* = 12.5 Hz, 1 H_{vinyl}), 6.82 (s, 1 H_{arom}), 6.93 (d, *J* = 12.5 Hz, 1 H_{vinyl}), 7.82 (s, 1 H_{arom})	33.5 (NCH_3), 102.7 (OCH_2O), 114.4 (CH), 112.9 (CH), 124.3 (CH), 128.8 (C), 130.9 (C), 137.8 (CH), 147.1 (C), 151.2 (C), 165.6 (C=O), 166.8 (C=O)
1f	oil	2.25 (s, 3 H, CH_3), 3.53 (s, 3 H, NCH_3), 6.11 (s, 2 H, OCH_2O), 6.75 (s, 1 H_{arom}), 6.96 (s, 1 H_{vinyl}), 7.69 (s, 1 H_{arom})	23.3 (CH_3), 34.1 (NCH_3), 102.4 (OCH_2O), 109.6 (CH), 112.0 (CH), 126.5 (C), 128.8 (C), 130.4 (C), 134.7 (CH), 150.5 (C), 152.0 (C), 166.2 (C=O), 168.5 (C=O)

[a] Satisfactory microanalyses obtained for new compounds: C ± 0.29, H ± 0.26, N ± 0.29.

Acknowledgment

This research was supported by the Centre National de la Recherche Scientifique, by MENESR and by the Program PRIM (Région Nord-Pas de Calais).

References

(1) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893.
(2) (a) Miller, W. H.; Alberts, D. P.; Bhatnagar, P. K.; Bondinell, W. E.; Callahan, J. F.; Calvo, R. R.; Cousins, R. D.; Erhard, K. F.; Heerding, D. A.; Keenan, R. M.; Kwon, C.; Manley, P. J.; Newlander, K. A.; Ross, S. T.; Samanen, J. M.; Uzinskas, I. N.; Venslavsky, J. W.; Yuan, C. C.-K.; Haltiwanger, R. C.; Gowen, M.; Hwang, S.-M.; James, I. E.; Lark, M. W.; Rieman, D. J.; Stroup, G. B.; Azzarano, L. M.; Salyers, K. L.; Smith, B. R.; Ward, K. W.; Johanson, K. O.; Huffman, W. F. *J. Med. Chem.* **2000**, *43*, 22. (b) Feuston, B. P.; Culberson, J. C.; Duggan, M. E.; Hartman, G. D.; Leu, C.-T.; Rodan, S. B. *J. Med. Chem.* **2002**, *45*, 5640.
(3) Vogt, B. R. US Patent 3985731, **1976**; *Chem. Abstr.* **1977**, *86*, 55304.
(4) Vogt, B. R. US Patent 38875441, **1975**; *Chem. Abstr.* **1975**, *83*, 131649.
(5) See for example: (a) Dieltiens, N.; Stevens, C. V.; Masschelein, K.; Hennebel, G.; van der Jeught, S. *Tetrahedron* **2008**, *64*, 4295. (b) Panayides, J.-L.; Pathak, R.; de Koning, C. B.; van Otterlo, W. A. L. *Eur. J. Org. Chem.* **2007**, 4953. (c) Kogen, H.; Toda, N.; Tago, K.; Marumoto, S.; Takami, K.; Ori, M.; Yamada, N.; Koyama, K.; Naruto, S.; Abe, K.; Yamazaki, R.; Hara, T.; Aoyagi, A.; Abe, Y.; Kaneko, T. *Org. Lett.* **2002**, *4*, 3359.
(6) (a) Walker, G. N. *J. Org. Chem.* **1972**, *37*, 3955. (b) Simchen, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 464. (c) Puar, M. S.; Vogt, B. R. *Tetrahedron* **1978**, *34*, 2887.
(7) Elvidge, J. A.; Jones, D. E. H. *J. Chem. Soc. C* **1967**, 2059.
(8) (a) Bestmann, H. J.; Shade, G.; Schmid, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 822. (b) Bestmann, H. J.; Shade, G.; Luetke, H.; Moenius, T. *Chem. Ber.* **1985**, *118*, 2640.
(9) For reviews, see: (a) Donohoe, T. J.; Orr, A. J.; Bingham, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 2664. (b) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (c) Grubbs, R. H. In *Handbook of Metathesis*, Vol. 1-3; Wiley-VCH: Weinheim, **2003**.
(10) For selected reviews, see: (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (b) Hoveyda, A. H. *Top. Organomet. Chem.* **1998**, *1*, 105. (c) Schrock, R. R. *Tetrahedron* **1999**, *55*, 8141. (d) Phillips, A. J.; Abell, A. D. *Aldrichimica Acta* **1999**, *32*, 75. (e) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012. (f) Hoveyda, A. H.; Schrock, R. R. *Chem. Eur. J.* **2001**, *7*, 945. (g) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (h) Connon, S. J.; Blechert, S. *Angew. Chem. Int. Ed.* **2003**, *42*, 1900. (i) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117. (j) Michaut, A.; Rodriguez, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 5740. (k) Schrock, R. R. *Angew. Chem. Int. Ed.* **2006**, *45*, 3748. (l) Grubbs, R. H. *Angew. Chem. Int. Ed.* **2006**, *45*, 3760.
(11) Howe, R. K.; Schleppnik, F. M. *J. Heterocycl. Chem.* **1982**, *4*, 721.
(12) Keck, G. E.; Boden, E.; Sonnewald, U. *Tetrahedron Lett.* **1981**, *22*, 2615.
(13) Roensch, H. *Eur. J. Biochem.* **1972**, *28*, 123.
(14) Pogosyan, G. M.; Karapetyan, T. G.; Matsoyan, S. G. *Armyanskii Khim. Zhur.* **1971**, *24*, 816; *Chem. Abstr.* **1972**, *76*, 86171.