Synthesis of Heterocyclic Compounds by Ring-Closing Metathesis (RCM): Preparation of Oxygenated or Nitrogenated Compounds

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Received 16 November 2005; revised 13 January 2006

Abstract: Novel methods for heterocyclic synthesis by metathesis have been developed. Versatile heterocyclic compounds were easily prepared in good yield from intermediate olefins by ring-closing olefin metathesis using the catalyst dichloro(benzylidene)bis(tricyclohexylphosphine)ruthenium.

Key words: ruthenium catalysts, ring-closing, olefin metathesis, heterocyclic systems

Olefin metathesis has been established as a very interesting, important and general reaction in synthetic organic chemistry and has attracted considerable attention in the last decade with respect to forming cyclic olefins. This reaction has been used in intramolecular cyclizations, which lead to the formation of N- and/or O-heterocyclic compounds.[1] The reaction proceeds through the formation of a new carbon–carbon bond from two olefin groups. Two C–C double bonds are cleaved and new C–C bonds are formed to give new compounds.

In general, acyclic olefin precursors can successfully undergo RCM to form five- to seven-membered ring system, but the preparation of products with larger heterocyclic rings is also achieved using olefin metathesis.[2] Metathesis has also seen a prolific use in the preparation of macrocyclic natural products from the corresponding diene substrates.[3]

The commercially available Grubbs' first-generation catalyst (Grubbs' carbene) has high functional-group tolerance and it is relatively moisture- and air-stable. The second-generation Grubbs' ruthenium catalyst possesses in general a very good application profile and shows enhanced RCM activity compared to its parent **I**, but it is more expensive.[4]

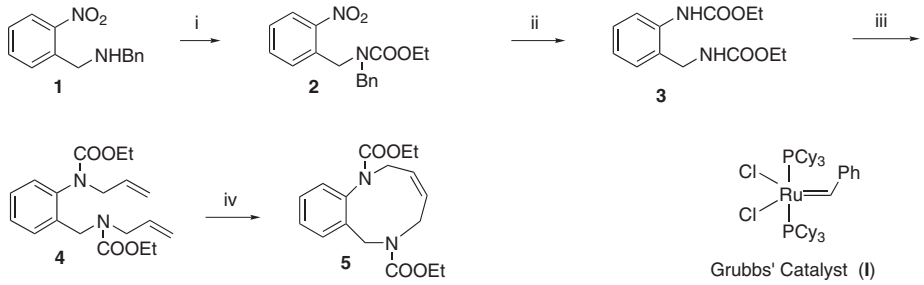
Recently, several investigations have been made in the field of the metathesis of various types of dienes.[5] In this paper, we describe an extension of RCM reaction to the synthesis of N- and/or O-heterocycles of nine, six and five atoms using a ruthenium catalyst and the reaction conditions. The metathesis reactions were carried out using dichloro(benzylidene)bis(tricyclohexylphosphine)ruthenium as catalyst in benzene at 60 °C. Treatment of dienes with Grubbs' catalyst under mild RCM conditions did not furnish the desired heterocyclic systems. We found that these dienes require vigorous conditions for ring closure. Among the various solvents (benzene, toluene and dichloromethane) and conditions tested, we found that benzene at 60 °C gave the best results (see Schemes 1– 4).

Initially we chose to synthesize nine-membered diazabenzo-fused heterocyclic compounds starting from the readily available bis-allyl compound **4**. The amine **1** was obtained from commercially available 2-nitrobenzyl chloride and benzylamine by conventional alkylation protocols.[6] Compound **1** was then converted into the nitrocarbamate **2**, by acylation using ethyl chloroformate according to established procedures.[7] Treatment of **2** with H_2/Pd-C yielded the reduced and debenzylated intermediate which afforded the bis-carbamate **3** after acylation with ethyl chloroformate. The resultant bis-carbamate **3** was then alkylated with allyl chloride under standard conditions to give **4** (Scheme 1). The diallyl **4** was subjected to RCM reaction using Grubbs' first generation catalyst. It is interesting to note, that all RCM reactions of this work were performed using the same concentration (see experimental). When TLC analysis confirmed consumption of the starting material, the reaction was stopped and subsequent silica gel column chromatography afforded the nine-membered benzo-fused 1,5-diazanine **5** (Scheme 1).

Under these optimized reaction conditions, we examined the application of RCM for other heterocyclic synthesis such as quinoline, *N*-arylpyrrole and furan compounds. Literature review revealed several RCM conditions for the synthesis of dihydroquinolines from different precursors using ruthenium catalyst.[8] Neither of these articles however provided the preparation of quinolines and quinolones from simple acetanilides using the dichloro(benzylidene)bis(tricyclohexylphosphine)ruthenium (**I**) as catalyst. We tried to synthesize the dihydroquinoline **10**, which is a useful heterocycle for the synthesis of biologically active compounds.

The crude diene **9** was prepared by dehydration of the corresponding hydroxyamide **8** using P_2O_5 under reflux conditions. Treatment of the hydroxyamide **8** with trifluoroacetic anhydride (TFA) afforded the tetrahydroquinolone **12** instead of the diene **9**. The compound **12** was formed by intramolecular cyclization of the acetamide group to the benzylic position. The alcohol **8** was prepared by direct *ortho*-lithiation of the acetamide **7** with

SYNTHESIS 2006, No. 11, pp 1823–1828
Advanced online publication: 05.05.2006
DOI: 10.1055/s-2006-942360; Art ID: Z22305SS

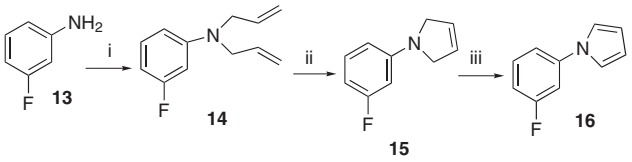


Scheme 1 *Reagents and conditions*: (i) ethyl chloroformate, Et_3N, CH_2Cl_2 (92%); (ii) a) H_2, Pd/C, MeOH (95%), b) ethyl chloroformate, Et_3N, CH_2Cl_2 (67%); (iii) NaH, allyl chloride, DMF (64%); (iv) with **I** (5 mol%), benzene, 60 °C (54%), with **I** (5 mol%), toluene, 60 °C (48%), with **I** (5 mol%), toluene, reflux (51%), with **I** (5 mol%), CH_2Cl_2, reflux (36%).

t-BuLi followed by treatment with acetaldehyde. RCM of the diene **9** afforded the 1,4-dihydroquinoline **10**. In the course of this reaction the acetyl protecting group was cleaved and the double bound isomerized. Immediately, the dihydroquinoline was readily converted to the quinoline **11**[9] in quantitative yield by treatment with Pd/C in decalin[10] (Scheme 2). Also was observed, that **10** was spontaneously oxidized to **11** on contact with oxygen, although more slowly than when the reaction mixture was treated with oxidative reagents.

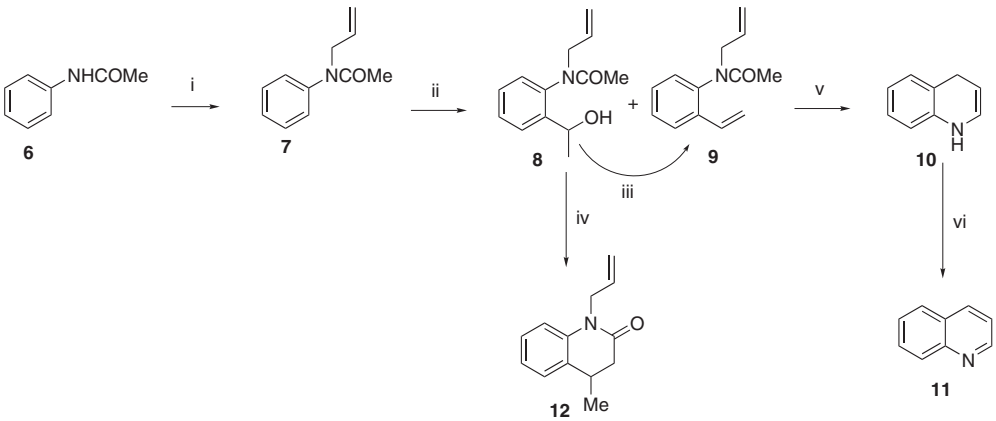
In the classical reactions, the most direct formation of pyrroles requires an enolizable 1,4-dicarbonylic compound (Paal–Knorr reaction), and usually require drastic reaction conditions.[11] More recently, Evans and coworkers[12] and Yang et al.[13] have prepared pyrrole nucleus using ruthenium-catalyzed RCM, and Stevens et al.[14] provided a more general RCM method using a combination of second generation Grubbs' catalyst and ruthenium(III) chloride.

In this context, we envisaged the possibility that *N*-arylpyrroles could be synthesized through RCM reaction of appropriate diallylanilines. The diallyl compound **14** was found to be an excellent substrate for RCM reaction to the formation of *N*-arylpyrrole. The *N*-(3-fluorophenyl)pyrrole (**16**) was prepared in three steps from commercially available 3-fluoroaniline (**13**) which was first converted into the tertiary amine **14** by standard methods and then subjected to RCM conditions. Finally the dehydrogenation of **15** with Pd/C in decalin leads to the *N*-arylpyrrole **16** (Scheme 3). The analytical data of **16** are in agreement with results described in the literature.[15]



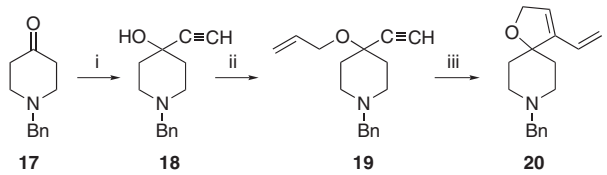
Scheme 3 *Reagents and conditions*: (i) NaH, allyl chloride, DMF (47%); (ii) with **I** (5 mol%), benzene, 60 °C (79%), with **I** (5 mol%), toluene, 60 °C (74%), with **I** (5 mol%), toluene, reflux (54%), with **I** (5 mol%), CH_2Cl_2, reflux (14%); (iii) Pd/C in decalin (89%).

Finally, the extension of this strategy towards the synthesis of spirofuropiperidines as potentially valuable functionalized 1,3-dienes from the *N*-benzyl-4-piperidone (**17**) was attempted. The strategy of our synthesis of the diene **20** is presented in Scheme 4. The dihydrofuran ring of **20** could be constructed at the last stage of the synthesis by RCM. The piperidone **17** was treated with lithium acetylide in THF at –78 °C to give after hydrolysis at room temperature the tertiary alcohol **18**. This alcohol was then reacted with allyl chloride to afford the allyloxy derivate **19**. The intramolecular enyne metathesis



Scheme 2 *Reagents and conditions*: (i) NaH, allyl chloride, DMF (50%); (ii) *t*-BuLi, CH_3CHO (50% for **8** and 15% for **9**); (iii) P_2O_5, CH_2Cl_2 (86%); (iv) $CF_3CO_2COCF_3$, toluene, r.t. (43%); (v) with **I** (5 mol%), benzene, 60 °C (52%), with **I** (5 mol%), toluene, 60 °C (45%), with **I** (5 mol%), toluene, reflux (41%), with **I** (5 mol%), CH_2Cl_2, reflux (32%); (**vi**) Pd/C in decalin (92%).

reaction[16] gives the formation of a new C–C bond between the internal C of the double bond and the internal C of the triple bond, and the alkylidene part of the alkene of **19** migrates onto the alkyne carbon to form a new diene moiety **20**.



Scheme 4 *Reagents and conditions*: (i) LiC_2H,THF, –78 °C (56%); (ii) NaH, allyl chloride, DMF (64%); (iii) with **I** (5 mol%), benzene, 60 °C (76%), with **I** (5 mol%), toluene, 60 °C (61%), with **I** (5 mol%), toluene, reflux (55%), with **I** (5 mol%), CH_2Cl_2, reflux (37%).

We have obtained in a straightforward manner, two new heterocyclic compounds from dialkenes or alkyne-alkenes using dichloro(benzylidene)bis(tricyclohexyl phosphine)ruthenium as catalyst. Several substrates were examined, and new heterocyclic systems containing five, six and nine atoms were prepared under the same reaction conditions. In addition to the novelty of the compounds prepared, this is the first report of the synthesis of spiro furopiperidines and 1,4-diazanine using metathesis methodology. This method is currently being applied to the synthesis of other heterocyclic systems, which might be intermediates for the preparation of biologically active compounds.

Melting points were obtained on an MFB-595010M Gallenkamp apparatus in open capillary tubes and are uncorrected. IR spectra were obtained using a FTIR PerkinElmer 1600 IR Spectrophotometer. Only noteworthy IR absorptions are listed (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 (200 and 50.3 MHz respectively) or Varian Gemini-300 (300 and 75.5 MHz) instrument using $CDCl_3$ as solvent with tetramethylsilane as internal standard or acetone-d_6. Other ^1H NMR spectra and heterocorrelation ^1H-^{13}C (HMQC and HMBC) experiments were recorded on a Varian VXR-500 (500 MHz). Mass spectra were recorded on a Hewlett-Packard 5988-A. Column chromatography was performed with silica gel (E. Merck, 70–230 mesh). Reactions were monitored by TLC using 0.25 mm silica gel F-254 (E. Merck). Microanalysis was determined on a Carlo Erba-1106 analyzer. All reagents were of commercial quality or were purified before use. Organic solvents were of analytical grade or were purified by standard procedures. Commercial products were obtained from Sigma-Aldrich.

N- or O-Allylation; General Procedure

To a stirred suspension of NaH (60%, 2 mmol) in distilled DMF (5 mL) were added the corresponding amine **3**, **6**, **13** or **18** or alcohol (1 mmol) and allyl chloride (5 mmol). The mixture was stirred for 6 h at 90 °C under argon. The mixture was warmed to r.t. and then allyl chloride was added three times (each 1 mmol) and heating was continued. Then the reaction mixture was hydrolyzed with H_2O (5 mL) and extracted with Et_2O (3 × 20 mL). The organic layer was washed with H_2O in order to remove the DMF. The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc) to give the corresponding *N*- or *O*-allyl derivative. The allylated compounds are listed below.

Ring-Closing Metathesis Reaction; General Procedure

Ru catalyst **I** (5 mol%) was added to a stirring solution of the requisite diene **4**, **9**, **14** or **19** in anhyd and degassed benzene (0.02 M) under argon. The mixture was heated at 60 °C until complete consumption of starting materials (TLC). The solution was concentrated under reduced pressure and purified by chromatography. Column chromatography of the residue on silica gel using appropriate mixture of EtOAc–hexane as eluent afforded analytically pure the corresponding heterocyclic system. Reaction time and temperature were optimized in each case. Yields indicated are for purified compounds. The products are listed below.

***N*-Benzyl-2-nitrobenzylamine (1)**

To a stirred solution of 2-nitrobenzyl chloride (2 g, 11.6 mmol) in distilled DMF (5 mL) were added the corresponding benzylamine (2.5 mL, 23.5 mmol) and K_2CO_3 (3.2 g, 23.5 mmol). The mixture was stirred for 6 h at 90 °C under argon and brought to r.t. Then the reaction mixture was hydrolyzed with H_2O (5 mL) and extracted with Et_2O (3 × 20 mL). The organic layer was washed with H_2O in order to remove the DMF. The combined organic layers were dried (Na_2SO_4), filtered and the solvent was removed under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc) to give the corresponding amine **1** as a yellow oil; yield: 2.17 g (77%).

IR (KBr): 3205, 1489, 1340, 1240 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.81 (s, 2 H, CH_2Ar), 4.05 (s, 2 H, CH_2Ar), 7.18–7.34 (m, 5 H, Ar), 7.43 (m, 3 H, Ar), 7.92 (d, *J* = 8 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 46.9 (*C*H_2Ar), 53.6 (*C*H_2Ar), 125.3 and 127.8 (C-3 and C-4), 127.0 (C-4′), 128.4 (C-2′, C-6′), 128.7 (C-3′ and C-5′), 129.5 (C-6), 133.8 (C-5), 134.7 and 137.1 (C-1 and C-1′), 148.5 (C-2).

Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.15; H, 6.03; N, 11.78.

***N*-Benzyl-*N*-ethoxycarbonyl-2-nitrobenzylamine (2)**

A mixture of the nitrobenzylamine (**1**; 1.0 g, 4.13 mmol), ethyl chloroformate (0.6 mL, 6.2 mmol) and Et_3N (0.9 mL, 6.2 mmol) in anhyd CH_2Cl_2 was stirred at r.t. for 24 h. Then the residue was extracted with CH_2Cl_2, dried (Na_2SO_4), filtered and the solvent removed. The crude of reaction was purified by silica gel column chromatography (hexane–EtOAc) to afford 1.2 g (92%) of **2** as a yellow oil.

IR (KBr): 1778, 1502, 1210 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.25 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.20 (q, *J* = 7.2 Hz, 2 H, CH_2O), 4.51 (s, 2 H, CH_2Ph), 4.80 (s, 2 H, CH_2Ph), 7.25–7.30 (m, 7 H, Ar), 7.60 (t, *J* = 8 Hz, 1 H, H-4), 8.05 (d, *J* = 8 Hz, 1 H, H-6).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.7 (CH_3), 47.2 (*C*H_2Ar), 50.8 (*C*H_2Ar), 61.9 (CH_2O), 125.0 and 127.5 (C-3 and C-4), 127.8 (C-4′), 128.4 (C-2′, C-6′), 128.6 (C-3′ and C-5′), 130.1 (C-6), 133.5 (C-5), 132.0 (C-1), 136.8 (C-1′), 148.2 (C-2), 156.8 (C=O).

2-(*N*-Ethoxycarbonylaminomethyl)-*N*-ethoxycarbonylaniline (3)

A solution of the nitro compound **2** (828 mg, 2.6 mmol) in MeOH (20 mL) was catalytically hydrogenated over 5% Pd/C (42 mg) at atmospheric pressure until the starting material was consumed (TLC). After removal of the catalyst by filtration, the filtrate was evaporated in vacuum to dryness. Pure 2-(*N*-ethoxycarbonylaminomethyl)aniline (537 mg, 95%) was obtained as a solid by chroma-

tography over a silica gel column (hexane–EtOAc); mp 78–80 °C (hexane–EtOAc).

2-(*N*-Ethoxycarbonylaminomethyl)aniline

IR (KBr): 3205, 1732, 1548, 1190 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.27 (t, *J* = 7 Hz, 3 H, CH_3), 4.25 (q, *J* = 7 Hz, 2 H, CH_2), 4.37 (s, 2 H, C*H*$_2$Ph), 6.62–6.70 (m, 2 H, H-4, H-6), 6.92 (m, 2 H, H-3, H-5).

A solution of the above intermediate aniline (853 mg, 4.4 mmol), ethyl chloroformate (0.62 mL, 6.5 mmol) and Et_3N (1.1 mL, 7.8 mmol) in anhyd CH_2Cl_2 (10 mL) was stirred at r.t. for 24 h. The mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried (Na_2SO_4), filtered and evaporated to dryness in vacuum. The residue was purified by silica gel column chromatography (hexane–EtOAc). The carbamate **3** was obtained as a yellow oil; yield: 778 mg (67%).

IR (KBr): 3308, 1743, 1645, 1570, 1167 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.26–1.34 (m, 6 H, CH_3), 4.14–4.38 (m, 4 H, CH_2), 4.38 (d, *J* = 5.6 Hz, 2 H, C*H*$_2$Ph), 6.20–6.50 (m, 1 H, H-4), 7.20–7.54 (m, 3 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.6 (CH_3), 14.7 (CH_3), 48.5 (*C*H_2Ar), 60.9 (CH_2O), 62.5 (CH_2O), 127.4 (C-6), 127.5 (C-4), 128.6 (C-5), 129.1 (C-3), 124.9 (C-2), 136.7 (C-1), 155.2 (C=O), 155.7 (C=O).

Anal. Calcd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N, 10.52. Found: C, 58.30; H, 6.45; N, 10.52.

2-(*N*′-Allyl-*N*′-ethoxycarbonylaminomethyl)-*N*-allyl-*N*-ethoxycarbonylaniline (4)

Starting from **3** (708 mg, 2.6 mmol) and following the general procedure of allylation, compound **4** was obtained as a colorless oil; yield: 587 mg (64%).

IR (KBr): 1724, 1534, 1203 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.25–1.28 (m, 6 H, CH_3), 3.81–3.97 (m, 2 H, CH_2N), 3.99–4.20 (m, 4 H, CH_2N), 4.22–4.40 (m, 4 H, CH_2O), 5.08 (d, *J* = 16 Hz, 4 H, CH_2=), 5.76–5.94 (m, 2 H, CH=), 7.02–7.29 (m, 4 H, H-3 to H-6).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.6 (CH_3), 14.7 (CH_3), 49.5 (*C*H_2Ar), 53.1 (2 × *C*H_2CH=), 61.6 (CH_2O), 61.7 (CH_2O), 118.3 (2 × CH_2=), 127.3, 127.7, 128.1, 128.5 (CH, Ar), 132.9 (2 × CH=), 134.0 (C-2), 138.5 (C-1), 156.8 (C=O).

Anal. Calcd for $C_{27}H_{30}N_2O_4$: C, 72.62; H, 6.77; N, 6.27. Found: C, 72.40; H, 6.54; N, 6.02.

1,6-Diethoxycarbonyl-2,5,6,7-tetrahydro-1*H*-1,6-benzodiazanine (5)

The diamino cyclized compound **5** was obtained as a colorless oil from the corresponding diallyl derivative **4** (100 mg, 0.3 mmol) following the general procedure described above for the RCM; yield: 60 mg (54%).

IR (KBr): 1213, 1415, 1678 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.26 (br s, 6 H, CH_3), 3.56 (s, 2 H, CH_2N), 3.95–4.12 (m, 2 H, CH_2N), 4.12–4.26 (m, 4 H, CH_2O), 4.29–4.37 (m, 2 H, CH_2N), 5.48–5.56 and 6.84–7.02 (m, 2 H, H-3, H-4), 7.12–7.30 (m, 4 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.6 and 14.7 (CH_3), 45.5, 49.4 and 52.0 (CH_2N), 61.7 (2 × CH_2O), 127.3, 127.8, 128.5, 128.9 (CH, Ar), 128.7 (CH=CH), 135.0 and 138.0 (C-7a, C-11a), 157.0 (C=O), 158.7 (C=O).

Anal. Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 62.89; H, 6.45; N, 8.97.

***N*-(Prop-2-enyl)acetanilide (7)**

Compound **7** was obtained from the acetanilide **6** (2 g, 15 mmol) by allylation following the general procedure described before; yield: 1.2 g (50%).

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.81 (s, 3 H, CH_3), 4.24 (dd, *J* = 1.2, 6.2 Hz, 2 H, CH_2N), 5.00–5.11 (m, 2 H, CH_2=), 5.75–5.85 (m, 1 H, CH=), 7.10 (d, *J* = 7.6 Hz, 2 H, H-2, H-6), 7.28–7.36 (m, 3 H, H-3, H-4, H-5).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.6 (CH_3), 52.0 (*C*H_2C), 117.7 (CH_2=), 127.7 (CH=), 127.9 (C-2, C-4), 129.5 (C-3, C-5), 133.0 (C-4), 142.8 (C-1), 169.9 (C=O).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.23; H, 7.18; N, 7.78.

***N*-Acetyl-2-(2-hydroxyethyl)-*N*-(prop-2-enyl)aniline (8) and *N*-(Prop-2′-enyl)-2-vinylacetanilide (9)**

A stirred solution of the starting acetanilide **7** (500 mg, 2.85 mmol) and TMEDA (0.9 mL, 5.7 mmol) in anhyd THF (5 mL) was cooled at –78 °C and a solution of *t*-BuLi was added (3.35 mL, 1.7 M, 5.7 mmol). The mixture was stirred under argon for 3 h, then an excess of acetaldehyde was added at –78 °C and allowed to warm slowly to r.t. over 12 h. A solution of aq sat. NH_4Cl was added (5 mL) and the mixture extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography (hexane–EtOAc) to give the alcohol **8** as the major product; yellow solid; yield: 340 mg (50%).

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.33 (d, *J* = 6.2 Hz, 3 H, CH_3), 2.52 (s, 3 H, CH_3CON), 4.21–4.29 (t, *J* = 8 Hz, 1 H, CHO), 7.18 (t, *J* = 8 Hz, 1 H, H-4), 7.30 (t, *J* = 8 Hz, 1 H, H-5), 7.24 (d, *J* = 8 Hz, 1 H, H-C), 7.48 (d, *J* = 8 Hz, 1 H, H-6), 7.80 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 23.0 (CH_3CO), 64.9 (CH_2O), 120.1 (C-6), 124.4 (C-4), 128.9 (C-3, C-5), 132.1 (C-2), 137.5 (C-1), 170.7 (C=O).

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.45; H, 7.65; N, 6.23.

The dehydrated compound **9** was obtained as a by-product; yellow oil; yield: 87 mg (15%).

9

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.73, 1.78 (s, 3 H, rotamers A and B, CH_3CON), 4.36 (d, *J* = 5.8 Hz, 2 H, CH_2N), 5.10–5.21 (m, 2 H, allyl CH_2=), 5.72-5.88 (m, 3 H, allyl CH=, vinyl CH_2=), 6.95–7.04 (m, 1 H, vinyl CH), 7.22–7.34 (m, 4 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 27.8 (CH_3CO), 52.3 (CH_2N), 117.5 (CH_2=), 117.6 (CH_2=), 122.7 (C-6), 128.1 (C-4), 128.8 and 129.2 (C-3, C-5), 132.0 (C-2), 133.1 (CH=), 141.5 (*C*H_2CH=), 142.0 (C-1), 166.0 (C=O).

Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.38; H, 7.30; N, 6.75.

1,4-Dihydroquinoline (10)

The dihydroquinoline **10** was obtained following the general procedure of RCM from the starting diene **9** (50 mg, 0.25 mmol); yield: 52%; yellow oil.

IR (KBr): 3021, 1523, 1498 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 4.46 (t, *J* = 1.8 Hz, 2 H, CH_2), 6.25–6.32 (m, 1 H, H-3), 7.12–7.20 (m, 2 H, NH, H-2), 7.38 (t, *J* = 8 Hz, 2 H, H-6, H-7), 7.70 (d, *J* = 7.6 Hz, 2 H, H-5, H-8).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 53.2 (CH_2), 118.5 and 118.8 (C-6, C-7), 124.2 (C-3), 128.5 (C-4a), 129.0 and 129.2 (C-5, C-8), 140.0 (C-8a), 142.1 (C-2).

Anal. Calcd for C_9H_9N: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.59; H, 6.75; N, 10.89.

Quinoline (11)

A solution of **10** (200 mg, 1.5 mmol) in decalin (5 mL) was added 5% Pd/C (10 mg). The resulting mixture was heated at 220 °C and stirred for 24 h. Finally the suspension was filtered and the solvent was removed by distillation. The purification by silica gel column chromatography (hexane–EtOAc) gave the quinoline (**11**) in 92% yield. The analytical data are in agreement with the results described for the commercial compound.[9]

***N*-Allyl-4-methyl-3,4-dihydro-1*H*-2-quinolone (12)**

A solution of the alcohol **8** (160 mg, 0.73 mmol) and trifluoracetic anhydride (0.5 mL) in toluene (5 mL) was stirred at r.t. for 24 h. The crude mixture was extracted with Et_2O (3 × 10 mL), dried (Na_2SO_4), filtered and concentrated. The purification by silica gel column chromatography (hexane–EtOAc) gave the unexpected 2-quinolone **12**; yellow oil; yield: 63.1 mg (43%).

IR (neat): 1728, 1495, 1345 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.32 (d, *J* = 6.2 Hz, 3 H, CH_3), 2.25 (dd, *J* = 1.8, 12 Hz, 1 H, CHC), 2.58 (dd, *J* = 6, 12 Hz, 1 H, CHC), 4.25–4.34 (m, 2 H, CH_2=), 5.10 (d, *J* = 8 Hz, 2 H, CH_2N), 5.48 (q, *J* = 6.2 Hz, 1 H, CH), 7.13–7.18 (m, 2 H, Ar), 7.40–7.46 (m, 2 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.1 (CH_3), 41.7 (CH_2), 52.2 (CH_2), 64.9 (CH), 118.3 (CH_2=), 128.0 (C-6), 128.1 (C-7), 128.3 (C-4a), 129.7 and 129.8 (C-5, C-8), 132.3 (CH=), 142.0 (C-8a), 172.5 (C=O).

Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.89; H, 7.31; N, 6.65.

***N*,*N*-Diallyl-*N*-(3-fluoro)aniline (14)**

From 3-fluoroaniline (1 g, 9 mmol), NaH (60% in mineral oil, 720 mg, 18 mmol) and allyl chloride (3.6 mL, 45 mmol), the diene **14** was obtained as an oil (528 mg, 47%). The corresponding monoallyl compound was also obtained under these conditions; yield: 360 mg (27%).

IR (KBr): 1540, 1210 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.90–3.93 (m, 4 H, CH_2N), 5.14–5.20 (m, 4 H, CH_2=), 5.80–5.90 (m, 2 H, CH=), 6.62–6.72 (m, 3 H, H-2, H-4, H-6), 7.15–7.25 (m, 1 H, H-5).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 52.8 (2 × CH_2N), 99.2 (*J* = 26 Hz, C-2), 102.5 (*J* = 22 Hz, C-4), 107.7 (*J* = 2.3 Hz, C-6), 116.1 (2 × *C*H_2=CH), 129.9 (*J* = 10.5 Hz, C-5), 133.3 (2 × CH=), 150.0 (C-1, *J* = 10 Hz), 162.1 (C-3, *J* = 251 Hz).

Anal. Calcd for $C_{12}H_{14}FN$: C, 75.36; H, 7.38; N, 9.93. Found: C, 74.99; H, 7.28; N, 9.62.

***N*-(3-Fluorophenyl)-2,5-dihydropyrrole (15) and *N*-(3-Fluorophenyl)pyrrole (16)**

The dihydropyrrole **15** was obtained starting from the diene **14** (100 mg, 0.5 mmol) and following the general procedure of RCM. The high instability of **15** gave spontaneously the pyrrole derivative **16**.

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Colorless oil; yield: 67 mg (79%).

IR (KBr): 1536, 1499, 1305, 720 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 4.08 (s, 4 H, CH_2), 5.94 (s, 2 H, CH=), 6.19–6.28 (m, 3 H, H-2′, H-4′, H-6′), 7.10–7.26 (m, 1 H, H-5′).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 62.6 (2 × CH_2N), 110.8 (C-3 and C-4), 111.2 (C-4′, *J* = 24 Hz), 118.9 (C-6′, *J* = 2.5 Hz), 123.9 (C-2′, *J* = 24.3 Hz), 130.1 (C-5′, *J* = 10.5 Hz), 139.6 (C-1′, *J* = 12 Hz), 148.2 (C-3′, *J* = 256 Hz).

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The analytical data of **16** are in agreement with the results described in the literature.[15]

***N*-Benzyl-4-ethynyl-4-hydroxypiperidine (18)**

To a stirred solution of *N*-benzyl-4-piperidone (**17**; 500 mg, 2.6 mmol) in anhyd THF (10 mL) under argon and cooled at –10 °C was slowly added lithium acetylide (359 mg, 3.9 mmol). The mixture was stirred for 20 min at –10 °C and allowed to warm to r.t. Then aq sat. NH_4Cl was added (5 mL) and the residue extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and the solvent removed. The silica gel column chromatography of the crude product (hexane–EtOAc) gave compound **18** as a yellow oil; yield: 305 mg (56%).

IR (KBr): 3323, 2210, 1589, 1415, 1234 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.85–1.98 (m, 4 H, CH_2C), 2.36–2.45 (m, 2 H, CH_2N*ax*), 2.50 (s, 1 H, C≡CH), 2.64–2.72 (m, 2 H, CH_2N*eq*), 3.52 (s, 2 H, CH_2Ar), 7.25–7.32 (m, 5 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 38.9 (*C*H_2C), 49.7 (CH_2N), 62.6 (CH_2), 72.5 (C–OH), 82.3 (*C*≡CH), 86.5 (C≡*C*H), 126.9 (C-4′), 128.2 (C-2′, C-6′), 128.9 (C-3′, C-5′), 132.4 (C-1′).

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.50. Found: C, 77.78; H, 7.59; N, 6.72.

***N*-Benzyl-4-ethynyl-4-(prop-2-enyloxy)piperidine (19)**

Compound **19** was obtained from the alcohol **18** (100 mg, 0.5 mmol) following the general procedure described above; yield: 75 mg (64%).

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.86–1.98 (m, 4 H, CH_2C), 2.35–2.46 (m, 2 H, CH_2N*ax*), 2.50 (s, 1 H, C≡CH), 2.60–2.70 (m, 2 H, CH_2N*eq*), 3.56 (s, 2 H, CH_2Ar), 4.11 (t, *J* = 5.6 Hz, 2 H, CH_2O), 5.15 (dd, *J* = 2, 16 Hz, 2 H, CH_2=), 5.84–6.02 (m, 1 H, CH=), 7.24–7.33 (m, 5 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 36.3 (CH_2C), 49.7 (CH_2N), 62.6 (CH_2), 64.6 (CH_2O), 75.5 (C–O), 76.6 (*C*≡CH), 96.3 (C≡*C*H), 116.4 (=CH_2), 127.0 (C-4′), 128.1 (C-2′, C-4′), 129.0 (C-3′, C-5′), 131.6 (C-1′), 135.0 (CH=).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.48. Found: C, 79.62; H, 8.09; N, 5.26.

Spiro(*N*-benzylpiperidine)-4,2′-(4′-vinyl-2′,5′-dihydrofuran) (20)

The spiro compound **20** was synthesized from **19** (16 mg, 0.06 mmol) following the general procedure of RCM; oil; yield: 13 mg (76%).

IR (KBr): 1523, 1251 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 1.96–2.04 (m, 4 H, CH_2C), 2.30–2.45 (m, 2 H, CH_2N*ax*), 2.75–2.85 (m, 2 H, CH_2N*eq*), 3.55 (s, 2 H, CH_2Ar), 4.59 (d, *J* = 1.8 Hz, 2 H, CH_2O), 5.15 (d, *J* = 12 Hz, 1 H, CH_2=), 5.55 (d, *J* = 20 Hz, 1 H, CH_2=), 5.85 (t, *J* = 2.4 Hz, 1 H, H-3), 6.20 (dd, *J* = 20, 12 Hz, 1 H, C=CH), 7.24–7.32 (m, 5 H, Ar).

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 40.2 (CH_2C), 48.2 and 51.2 (CH_2N), 64.1 (CH_2O), 94.1 (C-4), 110.8 (CH=*C*H_2), 126.8 (C-4″), 128.2 (C-2″, C-6″), 129.0 (C-3″, C-5″), 138.1 (C-1″), 133.2 (CH_2=*C*), 136.2 (CH=).

Anal. Calc. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.89; H, 7.99; N, 5.77.

Acknowledgment

Financial support for this work was provided by the Ministerio de Ciencia y Tecnología (MCYT, BQU 2002-00148), and the Comissionat per a Universitats i Recerca de la Generalitat de Catalunya, Spain (2005-SGR-00180).

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