Tetrahedron 69 (2013) 7234–7242

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Cross metathesis of several methylenecyclopentane derivatives

Pelayo Camps [a,b,*], Tània Gómez [a,b], M. Eugenia Budén [a,b], Ane Otermin [a,b],
Teresa Calvet [c], Mercè Font-Bardia [c,d]

[a] Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII 27-31, E-08028, Barcelona, Spain
[b] Institut de Biomedicina de la Universitat de Barcelona (IBUB), Universitat de Barcelona, Av. Joan XXIII 27-31, E-08028, Barcelona, Spain
[c] Departament de Cristalografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona, Martí Franquès s/n. E-08028 Barcelona, Spain
[d] Unitat de Difracció de RX, Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB), Universitat de Barcelona, Solé i Sabarís 1-3. E-08028 Barcelona, Spain

ARTICLE INFO

Article history:
Received 22 May 2013
Received in revised form 20 June 2013
Accepted 25 June 2013
Available online 1 July 2013

Keywords:
Homo cross metathesis
Hoveyda–Grubbs second generation catalysts
Tetrasubstituted alkenes
Configuration assignment
X-ray diffraction analyses

ABSTRACT

The cross metathesis (CM) of several methylenecyclopentane derivatives using Hoveyda–Grubbs second generation catalyst **4** (5–10 mol %) has been studied. Medium to good yields of tetrasubstituted alkenes have been obtained. In the case of 8-methyl-2,5-dimethylene-2,3,5,6-tetrahydro-1*H*,4*H*-3a,6a-(methanoiminomethano)pentalene-7,9-dione **2** products from single, double and triple CM were formed. With 8-methyl-5-methylene-5,6-dihydro-3a,6a-(methanoiminomethano)pentalene-2,7,9(1*H*,3*H*,4*H*)-trione **3** a good yield of the CM product was obtained working at 140 °C in xylene for 3 d, showing the high thermal stability of this catalyst. In the CM of diene **2** and enone **3**, the main products were always the *anti*-stereoisomers.

1. Introduction

In the last decade, the metathesis of olefins has become a very convenient method to prepare many kinds of alkenes,[1–9] and a key retrosynthetic pathway in the design of many organic syntheses.[10–14] Many di- and tri-substituted alkenes can be obtained by olefin metathesis. Also, several tetrasubstituted alkenes have been obtained by ring closing metathesis (RCM).[15–21] However, to the best of our knowledge, only a group has described the formation of tetrasubstituted alkenes by cross metathesis (CM), one of the partners being an α-methylene-β-lactam.[22,23]

We have recently described a one-step preparation of several methylenecyclopentane derivatives, such as compounds **1** and **2** from *N*-methylsuccinimide and 3-chloro-2-chloromethyl-1-propene.[24] Also, we have been interested for a long time in the preparation of belt compounds of general structure **6**.[25–28] Consequently, we considered of interest to study the CM of **1** (as a model compound), **2** and derivatives, such as **3**, as a possible way to prepare compounds **6** (Fig. 1).

2. Results and discussion

As a model reaction, compound **1** was heated in CH_2Cl_2 under an Ar atmosphere for 6 h plus 3 d at room temperature, in the presence of the Hoveyda–Grubbs second generation catalyst (**4**, 5% molar ratio), leading to a mixture of CM products *anti* or *Z* **7** and *syn* or *E* **8** (approximate ratio **7**/**8**=1:2) in 48% yield, much starting compound being recovered (Scheme 1). When this reaction was carried out at 45 °C for 66 h, the yield of mixture **7**+**8** increased till 79%, the ratio **7**/**8** being essentially the same. Pure samples of both stereoisomers could be isolated by silica gel column chromatography and were fully characterized, the stereochemistry of **7** and **8** was assigned on the basis of their epoxides.

Epoxidation of **7** gave only one epoxide **9** with C_s symmetry [10 ^{13}C NMR and 7 ^{1}H NMR signals: the signals of 4(6)-H_x and 4″(6″)-H_x appear overlapped]. The structure of this epoxide was clearly established by X-ray diffraction analysis (Fig. 2).[29] Consequently, the CM product **7** must be the (*Z*)-stereoisomer with C_{2h} symmetry, whose epoxidation can give only one epoxide. The CM product **8** must be the (*E*)-stereoisomer with C_{2v} symmetry. Since its C=C bond has diastereotopic faces, it might give two epoxides. However, epoxidation of **8** gave only one epoxide **10** that showed the same C_{2v} symmetry as **8** (five ^{13}C NMR and four ^{1}H NMR signals). The configuration of this epoxide was also established by X-ray

---

[*] Corresponding author. Tel.: +34 93 402 4536; fax: +34 93 403 5941; e-mail address: camps@ub.edu (P. Camps).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.06.092

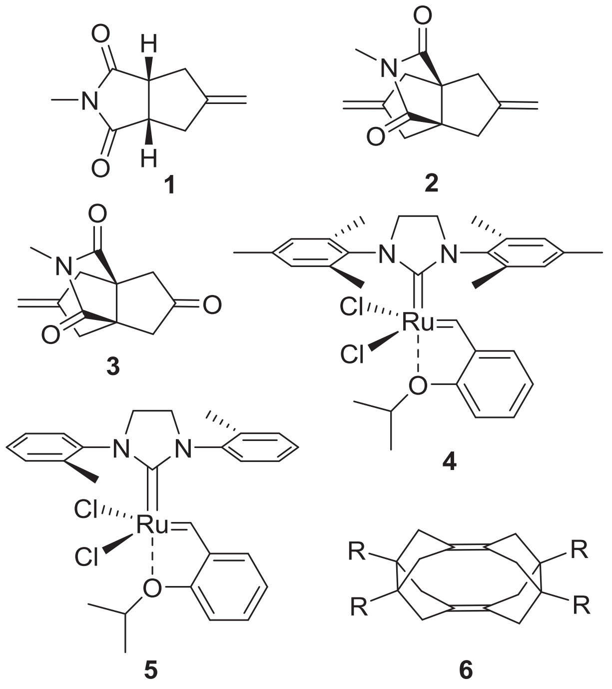
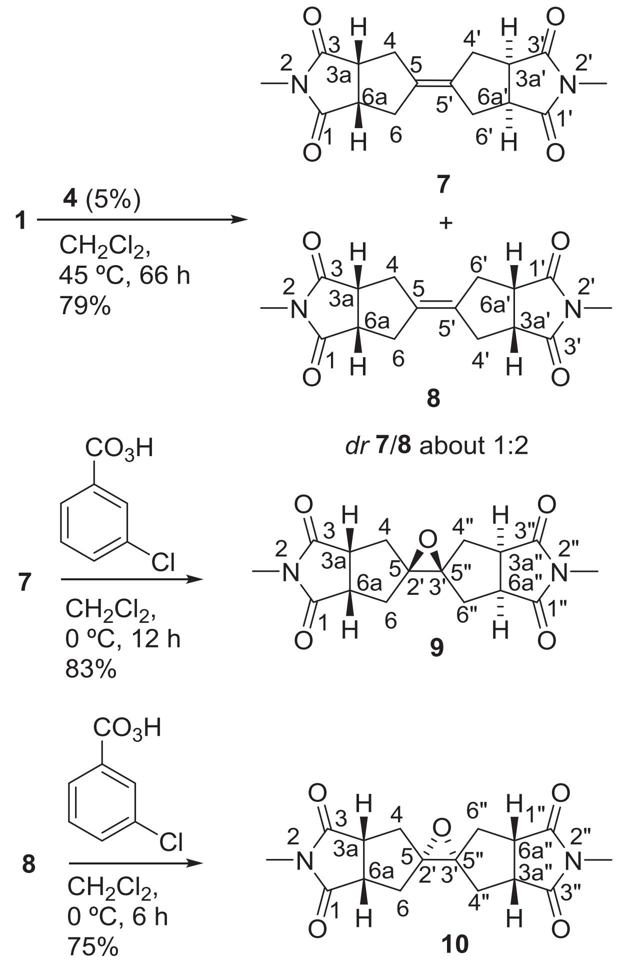


Fig. 1. Structure of methylenecyclopentane derivatives **1**, **2** and **3**, Hoveyda–Grubbs second generation catalyst **4**, Stewart–Grubbs catalyst **5** and belt compounds **6**.



Scheme 1. Metathesis of alkene **1** and epoxidation of the stereoisomeric alkenes **7** and **8**.

diffraction analysis (Fig. 3)[29] as that shown in Scheme 1, being the epoxide oxygen atom opposed to the bridgehead H atoms.

Similarly, heating a solution of diene **2** in a closed vessel in CH_2Cl_2 in the presence of catalyst **4** (5% molar ratio) for 5 d at 45 °C, a mixture of the single CM product **11** together with products derived from the CM of three (**12**) or four (**13**) units of the starting compound **2**, were obtained. These products were easily separated by silica gel column chromatography, isolating in order of elution, unreacted **2** (17% yield), **11** (29% yield), **12** (22% yield) and **13** (15% yield) (Scheme 2). Crude **11** was shown to be essentially only one stereoisomer, whose configuration was deduced to be *anti* or *Z*, as before, by chemoselective epoxidation of the more substituted C=C bond that gave epoxide **14** with C_s symmetry [15 ^{13}C NMR (the carbonyl carbon atoms were not differentiated) and 12 ^1H NMR signals] (Scheme 2). The fraction containing the product derived from the condensation of three units of **2** (**12**) also corresponded mainly to only one stereoisomer (^{13}C NMR). Crystallization from CH_2Cl_2/MeOH gave crystals adequate for X-ray diffraction analysis, which showed the product to be the *anti*,*anti*-stereoisomer, **12** (Fig. 4).[29] Compound **13** derived from the condensation of four units of **2** showed to be only one stereoisomer to which the *anti*,*anti*,*anti*-configuration was assigned on the basis of the established configuration of the formed C=C bonds in compounds **11** and **12** and its C_{2h} symmetry (15 ^{13}C NMR and 11 ^1H NMR signals).

We have also prepared enone **3** by controlled ozonization of **2**, followed by reduction of the ozonide with dimethyl sulfide (Scheme 3). Under the optimized conditions, **3** was obtained in 42% yield, together with the known[23] diketone **15** (33% yield) and starting diene **2**.

Heating enone **3** in the presence of Hoveyda–Grubbs catalyst **4** (5% molar) in CH_2Cl_2 (0.09 mmol **3**/mL) at 45 °C for 3 d in a closed vessel, a CM product **16** was obtained in only 4% yield (Scheme 4). When compound **3** was submitted to the above metathesis reaction conditions, but working in benzene at 80 °C or in xylene at 130 °C, the yield of **16** increased to 20% and 40%, respectively. When the reaction was carried out as before in xylene at 130 °C, but in a more concentrated solution (0.18 mmol **3**/mL), the yield increased to 45%. Worthy of note, metathesis of **3** under the last conditions, but using Stewart–Grubbs catalyst (**5**, 5% molar), which has been described as a better catalyst to prepare hindered alkenes, gave **6** in only 14% yield.

In the above reactions, part of the starting compound remained apparently unreacted (TLC). However, we established (^1H NMR) that working in xylene at 130 °C, the apparently unreacted compound **3** was in fact the isomerized product **18**, inadequate for the desired metathesis. A sample of **18** was obtained by reaction of compound **3** with triflic acid in CH_2Cl_2 solution.

Since, the metathesis process may be reversible we carried out the reaction in xylene (0.18 mmol **3**/mL) at 130 °C for 3 d in an open vessel, always using catalyst **4** (5% molar) and in the presence of *p*-quinone to reduce the isomerization of the exocyclic C=C bond,[30] thus obtaining **16** in 50% yield. When the reaction was carried out under the above conditions in a more concentrated solution (0.27 mmol **3**/mL), the yield of the above mixture increased to 65%. Finally, under the optimum reaction conditions found till present, the yield increased to 66% of analytically pure product by working in xylene at 140 °C for 3 d in an open vessel at a concentration of 0.52 mmol **3**/mL. The main component of the obtained mixture could be isolated in pure form as a white solid by heating the mixture with MeOH and separating the solid product. As before, the *anti* or *Z* configuration of the obtained product **16** was established by epoxidation, which gave epoxide **17** with C_s symmetry (14 ^{13}C NMR and 10 ^1H NMR signals) (Scheme 4).

All of the new compounds described in this paper have been fully characterized on the basis of their spectroscopic data (^1H NMR, ^{13}C NMR, IR), elemental analysis and accurate mass measurement.

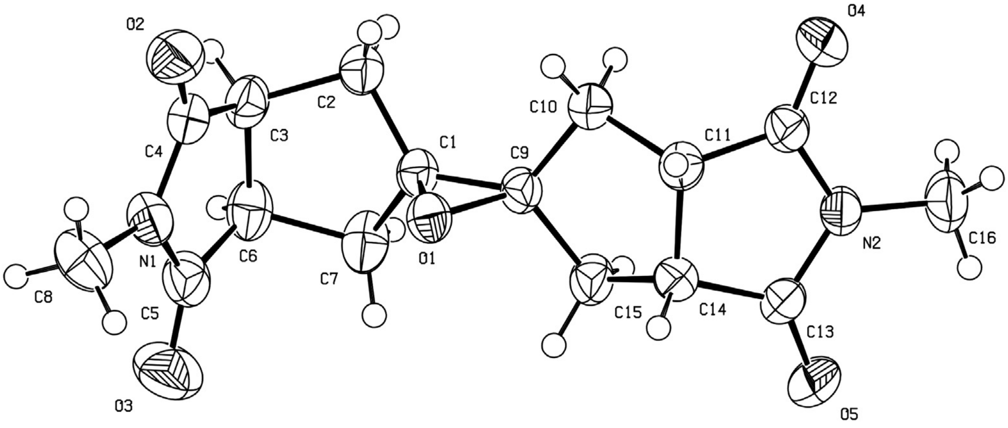


Fig. 2. ORTEP of compound **9**.

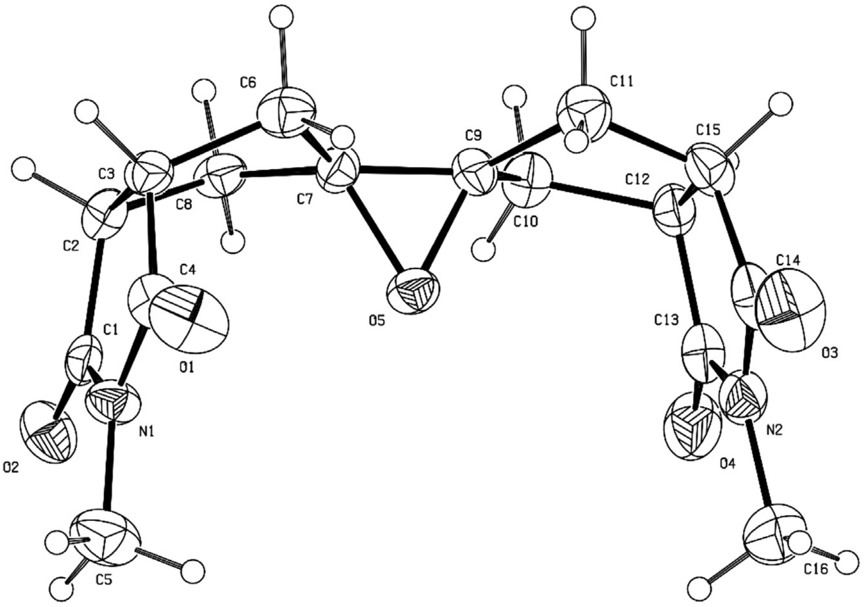


Fig. 3. ORTEP of compound **10**.

The ^{1}H and ^{13}C NMR spectra have been assigned on the basis of $^{1}H/^{1}H$ homocorrelation spectra (COSY and NOESY), $^{1}H/^{13}C$ heterocorrelation spectra [gHSQC (for one bond correlations) and gHMBC (for long range correlations)] and DEPT. Especially significant are the observed NOEs among protons of each diastereotopic moiety of epoxides **14** and **17**, which was the key to unequivocally assign the *Z* configuration to their precursor alkenes, **11** and **16**, respectively. Differentiation of the two moieties of epoxide **14** could be effected on the base of the NOE among 4(6)-H_n and 1″(3″)-H_x, which is not possible among 4″(6″)-H_n and 1(3)-H_x. The two moieties of epoxide **17** were assigned by comparison with the assignment carried out for epoxide **14**.

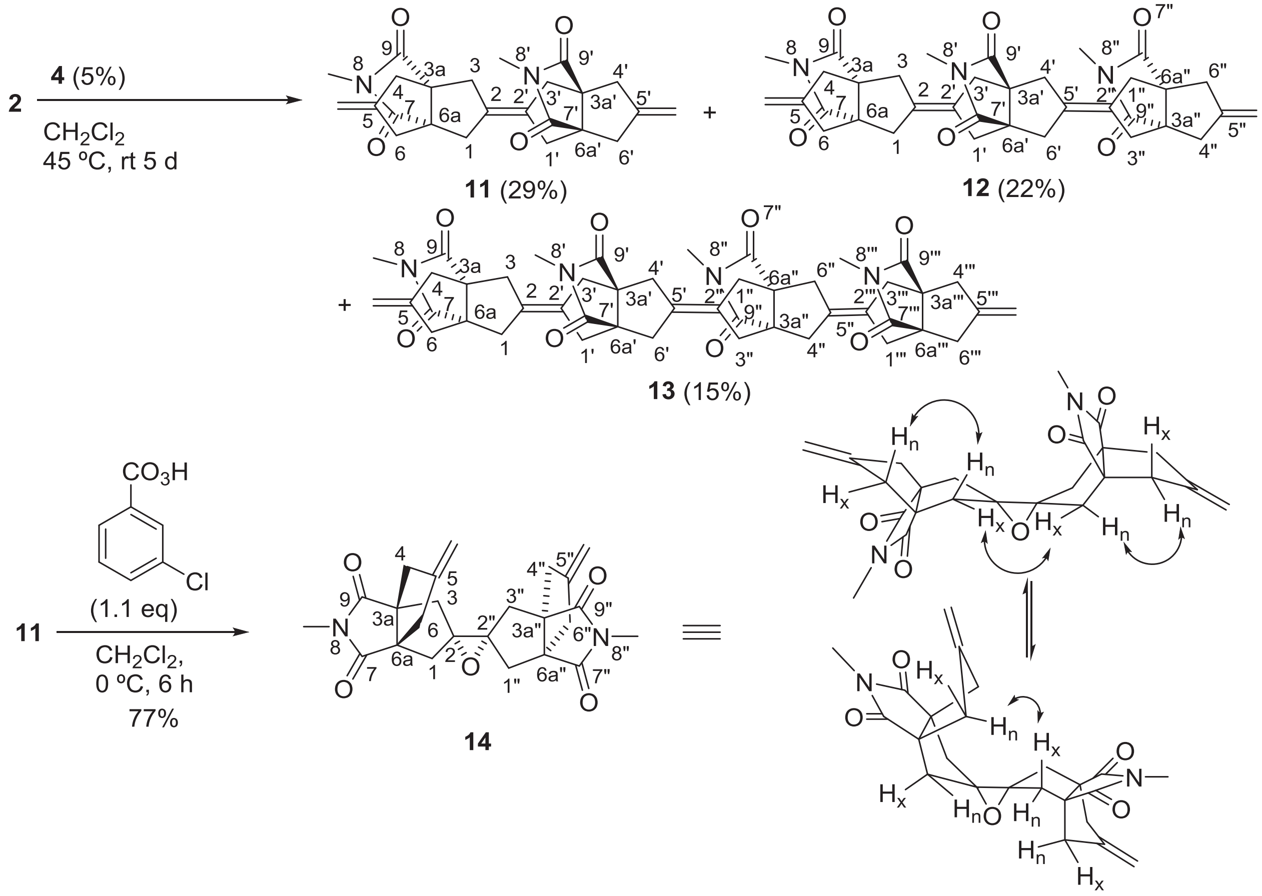
3. Conclusion

In conclusion, Hoveyda–Grubbs second generation catalyst **4** has shown to be adequate for the CM of methylenecyclopentane derivatives **1**, **2** and **3**, with formation of tetrasubstituted alkenes working at temperatures as high as 140 °C. Worthy of note, the main CM products, **11**, **12** and **13** derived from **2** and **16** derived from **3** has an *anti*-configuration for each formed C=C bond.

4. Experimental section

4.1. General experimental methods

Melting points were determined in open capillary tubes. Except where otherwise stated, the NMR spectra were performed in $CDCl_3$ at 400 MHz (^{1}H NMR) and 100.6 MHz (^{13}C NMR). Chemical shifts (δ) are reported in parts per million (ppm) related to internal TMS or $CDCl_3$. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad or their combinations. Assignments given for the NMR spectra are based on DEPT, $^{1}H/^{13}C$ single quantum correlation (gHSQC sequence), $^{1}H/^{13}C$ multiple bond correlation (gHMBC sequence) and Correlation SpectroscopY (COSY) experiments and also, for certain compounds, on Nuclear Overhauser Effect SpectroscopY (NOESY) information. Infrared spectra were obtained by using the Attenuated Total Reflectance (ATR) technique: Absorption values are given as wavenumbers (cm^{-1}), the intensity of the absorptions are given as strong (s), medium (m) or weak (w). High-resolution mass spectra (HRMS) were obtained with electrospray ionization using a TOF mass analyzer (ESI-MS) and are reported as *m*/*z* (relative ratio). Column



Scheme 2. Metathesis of diene **2** (arrows in compound **14** show significant NOEs. Geminal NOEs are not shown).

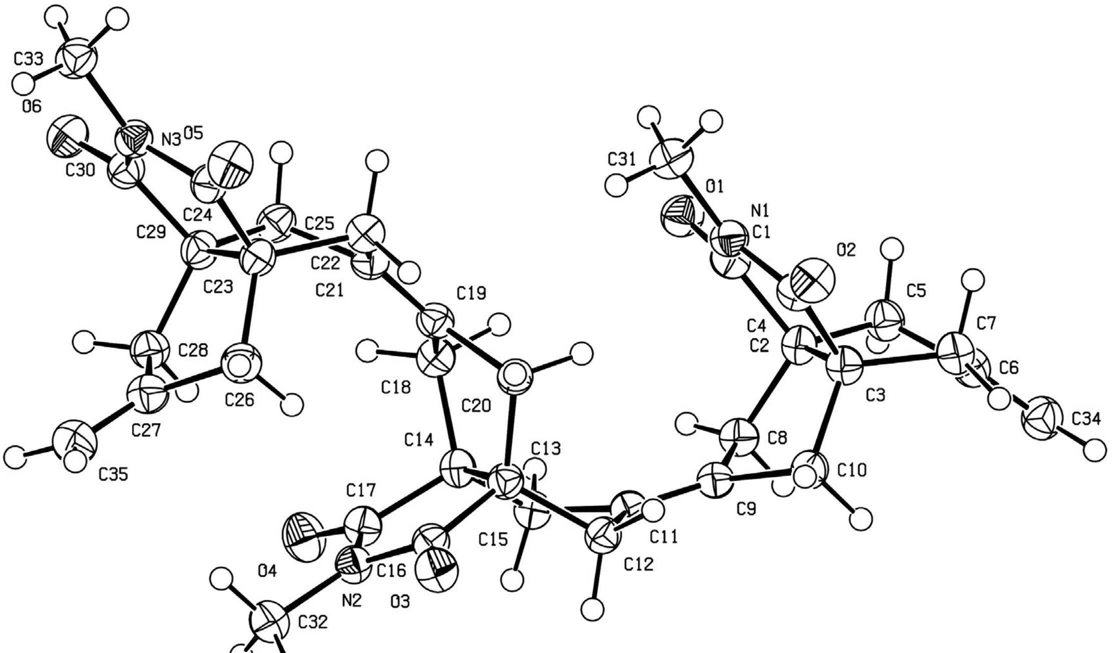
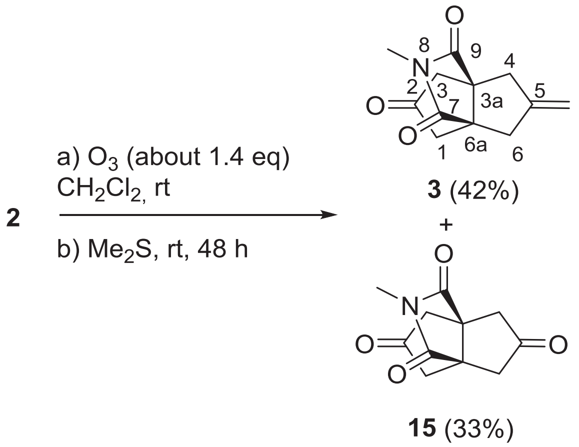


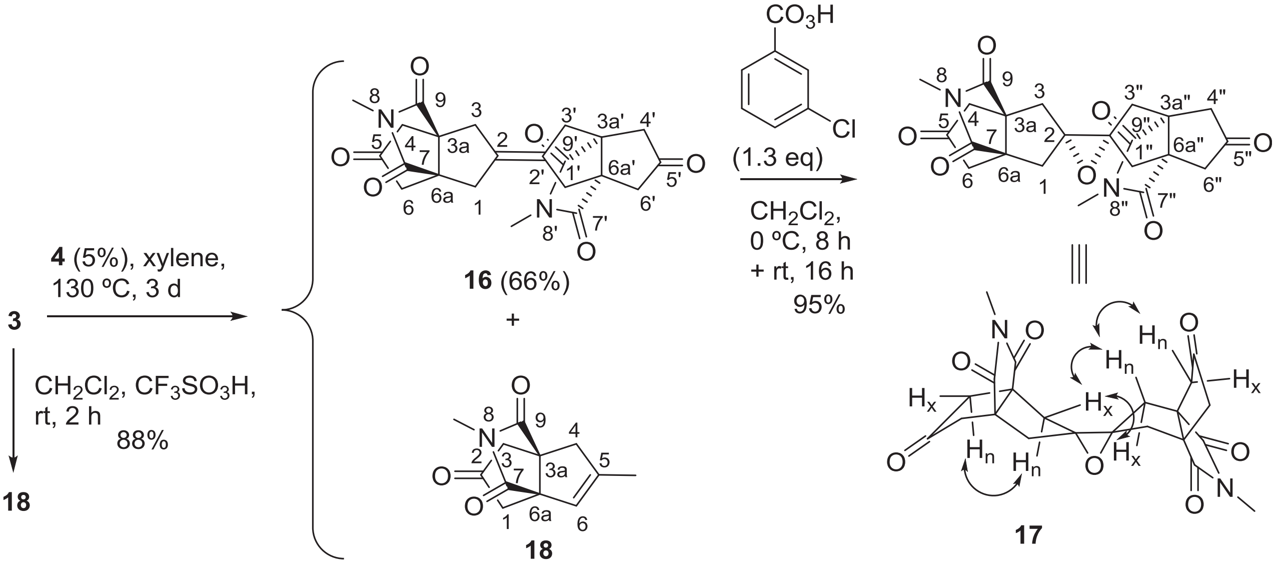
Fig. 4. ORTEP of compound **12**.

chromatography was performed on silica gel 60 A C.C (35–70 mesh) or basic Al_2O_3 (Brockmann activity Grade 1). The eluents employed are reported as volume/volume ratio. For the thin layer chromatography (TLC), aluminium-backed sheets with silica gel 60 F254 were used and spots were visualized with UV light and/or 1% aq $KMnO_4$.

The oxygen/ozone stream used to prepare compound **3** was generated with a Fisher Ozon 500 equipment. An oxygen stream



Scheme 3. Controlled ozonization of diene **2**.



Scheme 4. Metathesis of compound **3** (arrows in compound **17** show significant NOEs. Geminal NOEs are not shown).

(50 L/h) was passed through the ozonization equipment with a current of 0.20–0.22 A, and a production potency of 1.1, which corresponds to about 2.2 g ozone/h. Before starting the reaction, the oxygen/ozone stream was bubbled through CH_2Cl_2 for about 10 min, till the CH_2Cl_2 took a violet colour. In an empirical way, it was established that, under the above conditions, bubbling of the oxygen/ozone stream should last 10 min per gram of diene **2** in the solution.

Compound **2**, obtained as described,[23] contained about 11% of exocyclic C=C bonds isomerized to an endocyclic position (δ CH=C–CH_3=1.71 ppm; δ CH=C–CH_3=5.43 ppm). This product was purified by sublimation (60–100 °C/0.2–0.5 Torr) and crystallization from a small amount of MeOH (three times), till a content of about 0.3% isomerized exocyclic C=C bonds, before being used in the metathesis reaction. The mp of **2** increased from 91 – 92 °C, after sublimation, till 95–96.5 °C, after the third crystallization.

4.2. (3a*R*,3a′*R*,6a*S*,6a′*S*,*Z*) and (3a*R*,3a′*R*,6a*S*,6a′*S*,*E*)-2,2′-Dimethyl-3a,3a′,4,4′,6,6a′-octahydro-1*H*,1′*H*-[5,5′-bi(cyclopenta[*c*]pyrrolylidene)]-1,1′,3,3′(2*H*,2′*H*)-tetraone (7) and (8)

A solution of alkene **1** (758 mg, 4.6 mmol) in anhydrous CH_2Cl_2 (10 mL) and ruthenium catalyst **4** (144 mg, 0.23 mmol) was heated to 45 °C for 6 h under an Ar atmosphere and then the solution was magnetically stirred at room temperature for 3 d. The solvent was eliminated under reduced pressure and the brown oily residue (940 mg) was subjected to column chromatography (silica gel 35–70 μm, 25 g, hexane/EtOAc mixtures). In order of elution starting **1** (375 mg, hexane/EtOAc 85:15 till hexane/EtOAc 7:3) and a mixture of the CM products **7** and **8** (362 mg, hexane/EtOAc 1:1 till EtOAc), as a green-brown solid, were obtained. The above CM mixture was subjected to a new column chromatography (basic Al_2O_3, 7 g, hexane/EtOAc mixtures) to give a mixture of **7** and **8** in the approximate ratio **7**/**8**=1:2 (^{1}H NMR) (332 mg, 48% yield, hexane/EtOAc 7:3 till EtOAc) as a light brown solid. Crystallization of the above product from MeOH (7 mL) gave the analytical sample of this mixture as a white solid, mp 179–181 °C (MeOH). A part of the above mixture (147 mg) was subjected to column chromatography (silica gel 35–70 μm, 20 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 1:4, in order of elution, pure product **7** (20 mg), a mixture of **7** and **8** (96 mg) and slightly impure **8** (26 mg) were obtained. The mixture of **7** and **8** (96 mg) was subjected to a new column chromatography (silica gel 35–70 μm, 15 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 1:4, in order of elution, pure product **7** (12 mg), a mixture of **7** and **8** (55 mg) and slightly impure **8** (44 mg) were obtained. The last fraction (44 mg) was subjected to a new column chromatography (silica gel 35–70 μm, 5 g, hexane/EtOAc mixtures) to give a mixture of **7** and **8** (18 mg, hexane/EtOAc 1:1) and pure **8** (24 mg, hexane/EtOAc 1:1–1:4).

When a similar reaction was carried out, starting from **1** (704 mg, 4.26 mmol) and Ru catalyst **4** (134 mg, 0.21 mmol) in anhydrous CH_2Cl_2 (10 mL) and the solution was heated to 45 °C for 66 h, after concentration and silica gel chromatography, mixtures of CM products **7** and **8** in different ratios were obtained (543 mg, 79% global yield of the mixture, approximate global ratio **7**/**8**=1:2).

Analytical and spectroscopic data of **7**: R_f=0.33 (silica gel, 10 cm, EtOAc), mp 218–220 °C (hexane/EtOAc); IR (ATR) ν 2954 (w), 2919 (w), 2829 (w), 1766 (w), 1693 (s), 1681 (s), 1449 (m), 1427 (m), 1380 (m), 1308 (m), 1280 (m), 1182 (w), 1158 (w), 1101 (m), 995 (m), 968 (w), 958 (w), 651 (m), 611 (m) cm^{-1}; ^{1}H NMR δ 2.57 [d, *J*=16.4 Hz, 4H, 4(4′,6,6′)-H_x], 2.62–2.72 [complex signal, 4H, 4(4′,6,6′)-H_n], 2.95 (s, 6H, 2×*N*–CH_3), 3.24–3.30 [complex signal, 4H, 3a(3a′,6a,6a′)-H]; ^{13}C NMR δ 25.1 (CH_3, *N*–CH_3), 33.5 [CH_2, C4(4′,6,6′)], 44.9 [CH, C3a(3a′,6a,6a′)], 131.0 [C, C5(5′)], 179.8 (C, CON). HRMS (ESI) (*m*/*z*) calcd for $[C_{16}H_{18}N_2O_4+H]^+$: 303.1339. Found: 303.1346. Anal. Calcd for $C_{16}H_{18}N_2O_4\cdot 0.2H_2O$ (305.93): C, 62.82; H, 6.06; N, 9.16. Found: C, 62.70; H, 5.99; N, 8.83.

Analytical and spectroscopic data of **8**: R_f=0.28 (silica gel, 10 cm, EtOAc); mp 181–183 °C (hexane/EtOAc); IR (ATR) *ν* 2949 (w), 2918 (w), 2849 (w), 1766 (w), 1693 (s), 1432 (m), 1379 (m), 1307 (m), 1276 (m), 1182 (w), 1162 (w), 1093 (m), 1074 (w), 991 (s), 950 (w), 846 (w), 595 (m), 588 (m) cm^{-1}; ^{1}H NMR *δ* 2.58–2.64 [complex signal, 8H, 4(4′,6,6′)-H_x and 4(4′,6,6′)-H_n], 2.93 (s, 6H, *N*–CH_3), 3.25–3.29 [m, 4H, 3a(3a′,6a,6a′)-H]; ^{13}C NMR *δ* 25.0 (CH_3, 2×*N*–CH_3), 33.5 [CH_2, C4(4′,6,6′)], 44.8 [CH, C3a(3a′,6a,6a′)], 131.1 [C, C5(5′)], 179.6 (C, CON). HRMS (ESI) (*m*/*z*) calcd for $[C_{16}H_{18}N_2O_4+H]^+$: 303.1339. Found: 303.1343. Anal. Calcd for $C_{16}H_{18}N_2O_4\cdot 0.2H_2O$ (305.93): C, 62.82; H, 6.06; N, 9.16. Found: C, 63.21; H, 6.32; N, 8.53.

4.3. (2′*r*,3′*s*,3a*R*,3a″*R*,6a*S*,6a″*S*)-3a,3a″,4,4″,6,6″,6a,6a″-Octahydro-2,2″-dimethylcyclopenta[*c*]pyrrole-5-spiro-2′-oxirane-3′-spiro-5″-cyclopenta[*c*]pyrrole-1,1″,3,3″(2*H*,2″*H*)-tetraone (9)

To a cold (0 °C) solution of compound **7** (40 mg, 0.13 mmol) in CH_2Cl_2 (7.6 mL), *m*-chloroperbenzoic acid (38 mg, 77% content, 0.17 mmol) was added and the mixture was magnetically stirred at 0 °C for 6 h. More *m*-chloroperbenzoic acid (38 mg, 77% content, 0.17 mmol) was added and the mixture was stirred at 0 °C for 6 h more. The solution was filtered through neutral Al_2O_3 (1.3 g) washing with EtOAc (100 mL). The combined filtrate and washings were concentrated in vacuo to give epoxide **9** (35 mg, 83% yield) as a white solid. An analytical sample was obtained by crystallization of the above product from MeOH (2 mL), thus isolating **9** (25 mg) as a white solid, mp 192–194 °C (MeOH); IR (ATR) *ν* 2960 (w), 2934 (w), 2854 (w), 1767 (w), 1685 (s) (C=O st), 1432 (m), 1383 (m), 1311 (m), 1282 (m), 1076 (m), 991 (m), 598 (m) cm^{-1}; ^{1}H NMR *δ* 1.93 [d, *J*=14.4 Hz, 2H, 4(6)-H_n], 2.06–2.11 [dd, *J*=14.4 Hz, *J*′=3.6 Hz, 2H, 4″(6″)-H_n], 2.19–2.29 [complex signal, 4H, 4(6)-H_x and 4″(6″)-H_x], 2.98 (s, 3H, 2″-CH_3), 3.00 (s, 3H, 2-CH_3), 3.26–3.31 [m, 2H, 3a(6a)-H], 3.34–3.41 [m, 2H, 3a″(6a″)-H]; ^{13}C NMR *δ* 25.1 (CH_3, 2″-CH_3), 25.3 (CH_3, 2-CH_3), 31.1 [CH_2, C4″(6″)], 34.8 [CH_2, C4(6)], 42.9 [CH_2, C3a″(6a″)], 43.5 [CH_2, C3a(6a)], 68.2 (C, C5″), 71.2 (C, C5), 178.9 [C, C1″(3″)], 179.2 [C, C1(3)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{16}H_{18}N_2O_5+H]^+$: 319.1288. Found: 319.1292. Anal. Calcd for $C_{16}H_{18}N_2O_5\cdot 0.5H_2O$ (327.34): C, 58.71; H, 5.85; N, 8.56. Found: C, 58.66; H, 5.84; N, 8.19.

4.4. (2′*s*,3′*s*,3a*R*,3a″*R*,6a*S*,6a″*S*)-2,2″-Dimethyl-3a,3a″,4,4″,6,6″,6a,6a″-octahydrocyclopenta[*c*]pyrrole-5-spiro-2′-oxirane-3′-spiro-5″-cyclopenta[*c*]pyrrole-1,1″,3,3″(2*H*,2″*H*)-tetraone (10)

To a cold (0 °C) solution of compound **8** (19 mg, 63 μmol) in CH_2Cl_2 (3.5 mL), *m*-chloroperbenzoic acid (18 mg, 77% content, 80 μmol) was added and the mixture was magnetically stirred at 0 °C for 6 h. The solution was filtered through neutral Al_2O_3 (1.4 g) washing with EtOAc (50 mL). The combined filtrate and washings were concentrated in vacuo to give epoxide **10** (15 mg, 75% yield) as a white solid. An analytical sample was obtained by crystallization of the above product from CH_2Cl_2/MeOH 3:1 (0.4 mL), thus isolating **10** (12 mg) as a white solid, mp 246–248 °C (CH_2Cl_2/MeOH); IR (ATR) *ν* 2955 (w), 2924 (w), 2855 (w), 1768 (w), 1696 (s) (C=O st), 1432 (m), 1380 (m), 1289 (m), 1281 (m), 1082 (m), 999 (m), 812 (m), 596 (m) cm^{-1}; ^{1}H NMR (300 MHz) *δ* 1.95 [d, *J*=14.4 Hz, 4H, 4(4″,6,6″)-H_n], 2.35–2.44 [ddd, *J*=14.7 Hz, *J*′=8.1 Hz, *J*″=2.4 Hz, 4H, 4(4″,6,6″)-H_x], 2.98 [s, 6H, 2(2″)-CH_3], 3.24–3.32 [m, 4H, 3a(3a″,6a,6a″)-H]; ^{13}C NMR *δ* 25.4 [CH_3, 2(2″)-CH_3], 34.9 [CH_2, C4(4″,6,6″)], 43.5 [CH_2, C3a(3a″,6a,6a″)], 68.2 [C, C5(5″)], 178.1 [C, C1(1″,3,3″)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{16}H_{18}N_2O_5+H]^+$: 319.1288. Found: 319.1281. Anal. Calcd for $C_{16}H_{18}N_2O_5$ (318.33): C, 60.37; H, 5.70; N, 8.80. Found: C, 60.16; H, 5.71; N, 8.76.

4.5. (2*Z*,3a*R*,3a′*R*,6a*S*,6a′*S*)-8,8′-Dimethyl-5,5′-dimethylene-5,5′,6,6′-tetrahydro[2,2′-bi(3a,6a-(methanoiminomethano)pentalenylidene)]-7,7′,9,9′(1*H*,1′*H*,3*H*,3′*H*,4*H*,4′*H*,8*H*,8′*H*)-tetraone (11), (2*E*,2″*E*,3a*R*,3a″*R*,6a*S*,6a″*S*)-8,8′,8″-trimethyl-5,5″-dimethylene-5,5″,6,6″-tetrahydro-1′*H*-[2,2′:5′,2″-ter(3a,6a-(methanoiminomethano)pentalene)]-7,7′,7″,9,9′,9″(1*H*,1″*H*,3*H*,3′*H*,3″*H*,4*H*,4′*H*,4″*H*,6′*H*,8*H*,8′*H*,8″*H*)-hexaone (12) and (2*E*,2″*Z*,2‴*E*,3a*R*,3a′*S*,3a″*S*,3a‴*R*,6a*S*,6a′*R*,6a″*R*,6a‴*S*)-8,8′,8″,8‴-tetramethyl-5,5‴-dimethylene-5,5‴,6,6‴-tetrahydro-{2,2′:5′,2″:5″,2‴-quater[3a,6a-(methanoiminomethano)pentalene]}-7,7′,7″,7‴,9,9′,9″,9‴(1*H*,1′*H*,1″*H*,1‴*H*,3*H*,3′*H*,3″*H*,3‴*H*,4*H*,4′*H*,4″*H*,4‴*H*,6′*H*,6″*H*,8*H*,8′*H*,8″*H*,8‴*H*)-octaone (13)

A magnetically stirred solution of diene **2** (257 mg, 1.18 mmol, containing about 0.3% of isomerized C=C bond) and ruthenium catalyst **4** (37 mg, 59 μmol) in anhydrous CH_2Cl_2 (15 mL) was heated at 45 °C for 5 d under an Ar atmosphere. The solvent was eliminated under reduced pressure and the residue (300 mg) was subjected to column chromatography (silica gel 35–70 μm, 15 g, hexane/EtOAc mixtures) to give in order of elution: starting diene **2** [44 mg, 17% yield, about 0.6% isomerized C=C bond (^{1}H NMR), hexane/EtOAc 9:1], single CM product **11** as a beige solid (71 mg, 29% yield, about 10% isomerized C=C bond, hexane/EtOAc 7:3), double CM product **12** as a beige solid (51 mg, 22% yield, about 5% isomerized C=C bond, hexane/EtOAc 1:1) and triple CM product **13** as a brown solid (34.5 mg, 15% yield, about 5% isomerized C=C bond, hexane/EtOAc 3:7). The analytical sample of **11** (67 mg) was obtained as a white solid by crystallization of the impure product (105 mg, from two batches) from CH_2Cl_2 (0.5 mL) and MeOH (0.9 mL). The analytical sample of **12** (30 mg) was obtained as a white solid by crystallization of the impure product (35 mg) from CH_2Cl_2 (0.15 mL) and MeOH (0.3 mL). The analytical sample of **13** (27 mg) was obtained as a beige solid by crystallization of the impure product (34 mg) from CH_2Cl_2 (0.15 mL) and MeOH (0.3 mL).

Analytical and spectroscopic data of **11**: R_f=0.44 (silica gel, 8 cm, hexane/EtOAc 3:2); mp 205–206 °C (CH_2Cl_2/MeOH); IR (ATR) *ν* 2960 (w), 2928 (w), 2897 (w), 2839 (w), 1762 (w), 1703 (s) (C=O st), 1430 (m), 1370 (m), 1323 (m), 1270 (m), 1077 (m), 1017 (m), 1006 (m), 919 (m) cm^{-1}; ^{1}H NMR *δ* 2.31 [br d, *J*=16.0 Hz, 4H, 4(4′,6,6′)-H_n], 2.37 [d, *J*=14.0 Hz, 4H, 1(1′,3,3′)-H_n], 2.70 [d, *J*=14.4 Hz, 4H, 1(1′,3,3′)-H_x], 2.77 [d, *J*=16.0 Hz, 4H, 4(4′,6,6′)-H_x], 2.90 [s, 6H, 8(8′)-CH_3], 4.83 [m, 4H, C5(5′)=CH_2]; ^{13}C NMR *δ* 25.1 [CH_3, 8(8′)-CH_3], 40.0 [CH_2, C1(1′,3,3′)], 42.8 [CH_2, C4(4′,6,6′)], 60.5 [C, C3a(3a′,6a,6a′)], 109.7 [CH_2, C5(5′)=CH_2], 132.3 [C, C2(2′)], 147.1 [C, C5(5′)], 181.1 [C, C7(7′,9,9′)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{24}H_{26}N_2O_4+H]^+$: 407.1965. Found: 407.1955. Anal. Calcd for $C_{24}H_{26}N_2O_4\cdot 0.25H_2O$ (410.99): C, 70.14; H, 6.50; N, 6.82. Found: C, 70.31; H, 6.52; N, 6.57.

Analytical and spectroscopic data of **12**: R_f=0.28 (silica gel, 8 cm, hexane/EtOAc 3:2); mp 260–261 °C (CH_2Cl_2/MeOH); IR (ATR) *ν* 2953 (w), 2921 (w), 2850 (w), 1766 (w), 1691 (s) (C=O st), 1426 (m), 1377 (m), 1323 (m), 1276 (m), 1068 (m), 1017 (m) cm^{-1}; ^{1}H NMR *δ* 2.26–2.31 [complex signal, 8H, 1′(3′,4′,6′)-H_n and 4(4″,6,6″)-H_n], 2.39 [br d, *J*=16.0 Hz, 4H, 1(1″,3,3″)-H_n], 2.66 [br d, *J*=16.0 Hz, 4H, 1(1″,3,3″)-H_x], 2.76 [d, *J*=16.0 Hz, 4H, 1′(3′,4′,6′)-H_x], 2.79 [d, *J*=16.0 Hz, 4H, 4(4″,6,6″)-H_x], 2.88 (s, 3H, 8′-CH_3), 2.90 [s, 6H, 8(8″)-CH_3], 4.83 [s, 4H, 5(5″)=CH_2]; ^{13}C NMR *δ* 25.12 [CH_3, 8′-CH_3], 25.15 [CH_3, 8(8″)-CH_3], 39.9 [CH_2, C1(1″,3,3″)], 40.1 [CH_2, C1′(3′,4′,6′)], 42.9 [CH_2, C4(4″,6,6″)], 60.6 [C, C3a(3a″,6a,6a″)], 60.9 [C, C3a′(6a′)], 109.7 [CH_2, 5(5″)=CH_2], 132.2 [C, C2′(5′)], 132.6 [C, C2(2″)], 146.9 [C, C5(5″)], 180.98 [C, C7(7″,9,9″)], 181.00 [C, C7′(9′)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{35}H_{37}N_3O_6+NH_4]^+$: 613.3021. Found: 613.2993. Anal. Calcd for $C_{35}H_{37}N_3O_6\cdot 0.25H_2O$ (600.20): C, 70.04; H, 6.30; N, 7.00. Found: C, 69.84; H, 6.42; N, 6.91.

Analytical and spectroscopic data of **13**: R_f=0.15 (silica gel, 8 cm, hexane/EtOAc 3:2); mp 271–272 °C (dec, CH_2Cl_2/MeOH); IR (ATR) *ν*

2923 (w), 2849 (w), 1772 (w), 1692 (s), 1426 (m), 1376 (m), 1322 (m), 1273 (m), 1070 (m), 1021 (m), 904 (w), 728 (m) cm^{-1}; ^1H NMR δ 2.25 [d, *J*=16.4 Hz, 4H, 1′(3′,4″,6″)-H_n], 2.27 [d, *J*=16.2 Hz, 4H, 4(4‴,6,6‴)-H_n], 2.30 [d, *J*=15.2 Hz, 4H, 1″(3″,4′,6′)-H_n], 2.38 [d, *J*=16.6 Hz, 4H, 1(1‴,3,3‴)-H_n], 2.64 [d, *J*=16.6 Hz, 4H, 1(1‴,3,3‴)-H_x], 2.70 [d, *J*=15.2 Hz, 4H, 1″(3″,4′,6′)-H_x], 2.76 [d, *J*=16.4 Hz, 4H, 1′(3′,4″,6″)-H_x], 2.78 [d, *J*=16.2 Hz, 4H, 4(4‴,6,6‴)-H_x], 2.86 [s, 6H, 8(8‴)-CH_3], 2.89 [s, 6H, 8′(8″)-CH_3], 4.82 [s, 4H, 5(5‴)=CH_2]; ^{13}C NMR δ 25.12 [CH_3, 8′(8″)-CH_3], 25.14 [CH_3, 8(8‴)-CH_3], 39.9 [CH_2, C1(1‴,3,3‴)], 40.0 [CH_2, C1′(3′,4″,6″)], 40.2 [CH_2, C1″(3″,4′,6′)], 42.9 [CH_2, C4(4‴,6,6‴)], 60.6 [C, C3a(3a‴,6a,6a‴)], 61.1 [C, C3a′(3a″,6a′,6a″)], 109.7 [CH_2, 5(5‴)=CH_2], 132.0 [C, C2′(5″)], 132.6 [C, C2″(5′)], 146.9 [C, C5(5‴)], 180.9 [C, C7(7‴,9,9‴)], 181.0 [C, C7′(7″,9′,9″)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{46}H_{48}N_4O_8+H]^+$: 785.3545. Found: 785.3552. Anal. Calcd for $C_{46}H_{48}N_4O_8\cdot H_2O$ (802.92): C, 68.81; H, 6.28; N, 6.98. Found: C, 68.98; H, 6.52; N, 6.49.

4.6. (2*r*,2″*s*,3a*R*,3a″*R*,6a*S*,6a″*S*)-8,8″-Dimethyl-5,5″-dimethylene-5,5″,6,6″-tetrahydro-3a,6a;3a″,6a″-bi[(methanoiminomethano)pentalene]-2-spiro-2′-oxirane-3′-spiro-2″-pentalene-7,7″,9,9″(1*H*,1″*H*,3*H*,3″*H*,4*H*,4″*H*,8*H*,8″*H*)-tetraone (14)

To a cold (0 °C) solution of compound **11** (135 mg, 0.33 mmol) in CH_2Cl_2 (4.5 mL), *m*-chloroperbenzoic acid (82 mg, 77% content, 0.37 mmol) was added and the mixture was magnetically stirred at 0 °C for 6 h. The solution was concentrated in vacuo, the residue was taken in EtOAc (2 mL) and was filtered through neutral Al_2O_3 (4 g) washing with EtOAc (120 mL). The combined filtrate and washings were concentrated in vacuo to give a solid (153 mg) that was subjected to column chromatography (silica gel 35–70 μm, hexane/EtOAc mixtures). On elution with hexane/EtOAc 7:3, epoxide **14** (108 mg, 77% yield) was isolated as a light brown solid. An analytical sample of **14** (34 mg) was obtained as a white solid by crystallization of the above product (51 mg) from CH_2Cl_2/MeOH 2:9 (1.1 mL). R_f=0.30 (silica gel, 9.5 cm, hexane/EtOAc 1:1); mp 175–176 °C (CH_2Cl_2/MeOH); IR (ATR) ν 2960 (w), 2907 (w), 2849 (w), 1773 (w), 1696 (s) (C=O st), 1425 (m), 1375 (m), 1327 (m), 1274 (m), 1094 (m), 1069 (m), 1027 (m), 1017 (m), 910 (m), 888 (m), 735 (m), 720 (m) cm^{-1}; ^1H NMR δ 1.939 [d, *J*=14.8 Hz, 2H, 1(3)-H_n], 1.942 [d, *J*=14.4 Hz, 2H, 1″(3″)-H_n], 2.14 [d, *J*=14.8 Hz, 2H, 1(3)-H_x], 2.24 [d, *J*=14.4 Hz, 2H, 1″(3″)-H_x], 2.40 [d, *J*=15.2 Hz, 2H, 4(6)-H_n], 2.58 [dt, *J*=16.4 Hz, *J*′=2.0 Hz, 2H, 4″(6″)-H_n], 2.73 [d, *J*=15.2 Hz, 2H, 4(6)-H_x], 2.82 [d, *J*=16.4 Hz, 2H, 4″(6″)-H_x], 2.95 (s, 3H, *N*–CH_3), 2.98 (s, 3H, *N*–CH_3), 4.85–4.87 (m, 2H, 5″=CH_2), 4.88–4.90 (m, 2H, 5=CH_2); ^{13}C NMR δ 25.2 (CH_3, *N*–CH_3), 25.3 (CH_3, *N*–CH_3), 39.5 [CH_2, C1″(3″)], 41.2 [CH_2, C1(3)], 42.7 [CH_2, C4(6)], 42.8 [CH_2, C4″(6″)], 59.4 [C, C3a″(6a″)], 60.0 [C, C3a(6a)], 69.5 (C, C2), 71.0 (C, C2″), 110.0 (5″=CH_2), 110.4 (5=CH_2), 146.2 (C, C5″), 147.0 (C, C5), 180.6 [C, C7(9) and C7″(9″)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{24}H_{26}N_2O_5+NH_4]^+$: 440.2180. Found: 440.2175. Anal. Calcd for $C_{24}H_{26}N_2O_5$ (422.48): C, 68.23; H, 6.20; N, 6.63. Found: C, 68.09; H, 6.13; N, 6.43.

4.7. (3a*R*,6a*S*)-8-Methyl-5-methylene-5,6-dihydro-3a,6a-(methanoiminomethano)pentalene-2,7,9(1*H*,3*H*,4*H*)-trione (3)

An oxygen/ozone stream, providing about 2.2 g ozone/h, was bubbled through a cold (0 °C) solution of diene **2** (201 mg, 925 μmol) in CH_2Cl_2 (40 mL) for 2 min. After addition of Me_2S (6.52 mL, 1.69 g, 27.2 mmol), the mixture was stirred at room temperature for 48 h. The volatile products were eliminated in vacuo and the residue (303 mg) was subjected to column chromatography (silica gel 35–70 μm, 18 g, hexane/EtOAc mixtures). In order of elution, starting **2** (62 mg, hexane/EtOAc 4:1), enone **3** (86 mg, 42% yield, hexane/EtOAc 7:3) and diketone **15** (69 mg, 33% yield, hexane/EtOAc 7:2 till 1:1) were isolated as white solids. The analytical sample of **3** (63 mg, 31% yield, containing about 3% isomerized C=C bonds) was obtained by sublimation (110 °C/0.2–0.5 Torr) of the above product. R_f=0.34 (silica gel, 10 cm, hexane/EtOAc 1:1); mp 135–137 °C (sublimed at 110 °C/0.2–0.5 Torr); IR (ATR) ν 2949 (w), 2923 (w), 1770 (w), 1736 (m), 1684 (s) (C=O st), 1431 (m), 1380 (m), 1328 (m), 1280 (m), 1172 (m), 1077 (m), 1010 (m), 920 (m), 631 (m) cm^{-1}; ^1H NMR δ 2.54 [dt, *J*=16.4 Hz, *J*′=2.0 Hz, 2H, 4(6)-H_n], 2.58 [d, *J*=20.0 Hz, 2H, 1(3)-H_n], 2.85 [d, *J*=20.0 Hz, 2H, 1(3)-H_x], 2.98 (s, 3H, *N*–CH_3), 3.00 [dm, *J*=16.4 Hz, 2H, 4(6)-H_x], 4.93 (tt, *J*=2.2 Hz, *J*′=1.4 Hz, 2H, C5=CH_2); ^{13}C NMR δ 25.5 (CH_3, *N*–CH_3), 44.1 [CH_2, C4(6)], 46.9 [CH_2, C1(3)], 56.7 [C, C3a(6a)], 110.7 (CH_2, C5=CH_2), 145.0 (C, C5), 180.0 [C, C7(9)], 212.7 (C, C2). HRMS (ESI) (*m*/*z*): calcd for $[C_{12}H_{13}NO_3+H]^+$: 220.0968. Found: 220.0968. Anal. Calcd for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.98; N, 6.39. Found: C, 65.76; H, 5.93; N, 6.23.

4.8. (3a*R*,3a′*R*,6a*S*,6a′*S*,*Z*)-8,8′-Dimethyl-[2,2′-bi(3a,6a-methanoiminomethano)pentalenylidene]-5,5′,7,7′,9,9′(1*H*,1′*H*,3*H*,3′*H*,4*H*,4′*H*,6*H*,6′*H*,8*H*,8′*H*)-hexaone (16)

A magnetically stirred solution of enone **3** (58 mg, 0.26 mmol, containing about 3% of isomerized C=C bonds) and ruthenium catalyst **4** (8.5 mg, 13 μmol) in anhydrous xylene (0.5 mL) was heated at 130–140 °C for 3 d under an Ar atmosphere. The solvent was eliminated under reduced pressure and the residue (78 mg) was subjected to column chromatography (silica gel 35–70 μm, 3.5 g, hexane/EtOAc mixtures) to give in order of elution: a mixture of enones **3** and **18** (6 mg, ratio **3**/**18** 1:1.6, hexane/EtOAc 7:3) and CM product **16** (56 mg, hexane/EtOAc 1:4 to EtOAc). The above product **16** was heated under reflux with MeOH (0.5 mL). The mixture was allowed to cool and was decanted to give the analytical sample of **16** (35 mg, 66% yield) as a white solid. R_f=0.47 (silica gel, 8 cm, EtOAc); mp>300 °C (MeOH); IR (ATR) ν 2949 (w), 2914 (w), 1773 (w), 1747 (m), 1739 (s), 1697 (s) (C=O st), 1432 (m), 1380 (m), 1323 (m), 1272 (m), 1170 (m), 1065 (m), 998 (m) cm^{-1}; ^1H NMR δ 2.50 [br d, *J*=14.8 Hz, 4H, 1(1′,3,3′)-H_n], 2.51 [d, *J*=20.0 Hz, 4H, 4(4′,6,6′)-H_n], 2.86 [d, *J*=20.0 Hz, 4H, 4(4′,6,6′)-H_x], 2.97 [br d, *J*=14.8 Hz, 4H, 1(1′,3,3′)-H_x], 2.99 (s, 6H, 2*N*–CH_3); ^{13}C NMR δ 25.6 (CH_3, *N*–CH_3), 41.4 [CH_2, C1(1′,3,3′)], 46.9 [CH_2, C4(4′,6,6′)], 57.1 [C, C3a(3a′,6a,6a′)], 131.6 [C, C2(2′)], 179.6 [C, C7(7′,9,9′)], 212.0 [C, C5(5′)]. HRMS (ESI) (*m*/*z*): calcd for $[C_{22}H_{22}N_2O_6+NH_4]^+$: 428.1816. Found: 428.1808. Anal. Calcd for $C_{22}H_{22}N_2O_6\cdot 0.75H_2O$ (423.94): C, 62.33; H, 5.59; N, 6.61. Found: C, 62.39; H, 5.47; N, 6.46.

4.9. (2*r*,2″*s*,3a*R*,3a″*R*,6a*S*,6a″*S*)-8,8″-Dimethyl-3a,6a;3a″,6a″-bi[(methanoiminomethano)pentalene]-2-spiro-2′-oxirane-3′-spiro-2″-pentalene-5,5″,7,7″,9,9″(1*H*,1″*H*,3*H*,3″*H*,4*H*,4″*H*,6*H*,6″*H*,8*H*,8″*H*)-hexaone (17)

To a cold (0 °C) solution of compound **16** (73 mg, 0.18 mmol) in CH_2Cl_2 (12.5 mL), *m*-chloroperbenzoic acid (60 mg, 77% content, 0.27 mmol) was added and the mixture was magnetically stirred at 0 °C for 8 h and at room temperature for 16 h. The solution was washed with saturated aqueous solution of $NaHCO_3$ (3×15 mL), dried with anhydrous Na_2SO_4 and concentrated in vacuo to give epoxide **17** (78 mg) as a light brown solid. The analytical sample of **17** (72 mg, 95% yield) was obtained as a white solid by heating the solid with hexane (0.3 mL), mp 271–272 °C (dec, hexane); IR (ATR) ν 2920 (w), 1770 (w), 1743 (m), 1694 (s) (C=O st), 1431 (m), 1380 (m), 1325 (m), 1279 (m), 1173 (m), 1073 (m), 1013 (m) cm^{-1}; ^1H NMR δ 2.04 [d, *J*=14.8 Hz, 2H, 1″(3″)-H_n], 2.15 [d, *J*=14.8 Hz, 2H, 1(3)-H_n], 2.34 [d, *J*=14.4 Hz, 2H, 1(3)-H_x], 2.49 [d, *J*=14.8 Hz, 2H, 1″(3″)-H_x], 2.56 [d, *J*=20.0 Hz, 2H, 4(6)-H_n], 2.70 [d, *J*=19.6 Hz, 2H, 4″(6″)-H_n], 2.86 [d, *J*=20.0 Hz, 2H, 4(6)-H_x], 2.87 [d, *J*=20.0 Hz, 2H, 4″(6″)-H_x], 2.99 (s, 3H, 8″-CH_3), 3.03 (s, 3H, 8-CH_3); ^{13}C NMR δ 25.6 (CH_3, 8″-CH_3), 25.9 (CH_3, 8-CH_3), 40.9 [CH_2, C1″(3″)], 42.9 [CH_2, C1(3)], 46.8

[CH_2, C4″(6″)], 46.9 [CH_2, C4(6)], 56.07 [C, C3a(6a)], 56.09 [C, C3a″(6a″)], 69.3 (C, C2), 69.6 (C, C2″), 179.0 [C, C7″(9″)], 179.5 [C, C7(9)], 211.4 (C, C5″), 211.8 (C, C5). HRMS (ESI) (*m*/*z*): calcd for $[C_{22}H_{22}N_2O_7+NH_4]^+$: 444.1765. Found: 444.1760. Anal. Calcd for $C_{22}H_{22}N_2O_7\cdot 1.5H_2O$ (453.45): C, 58.27; H, 5.56; N, 6.18. Found: C, 58.42; H, 5.73; N, 5.70.

4.10. (3a*R**,6a*R**)-5,8-Dimethyl-3a,6a-(methanoiminomethano)pentalene-2,7,9(1*H*,3*H*,4*H*)-trione (18)

To a solution of enone **3** (60 mg, 0.27 mmol) in anhydrous CH_2Cl_2 (6 mL) triflic acid (21 mg, 0.14 mmol) was added and the mixture was stirred under an Ar atmosphere at room temperature for 2 h. Solid K_2CO_3 (70 mg) was added, the solution was filtered and the solid was washed with CH_2Cl_2 (3×2 mL). The combined filtrate and washings were concentrated in vacuo to give enone **18** (65 mg) as a beige solid, which on sublimation (110–110 °C/0.2–0.5 Torr) gave **18** (53 mg, 88% yield) as a white solid. R_f=0.40 (silica gel, 9 cm, hexane/EtOAc 2:3); mp 137–138 °C (sublimed at 100–110 °C/0.2–0.5 Torr); IR (ATR) ν 2944 (w), 2921 (w), 1768 (w), 1733 (m), 1691 (s) (C=O st), 1430 (m), 1383 (m), 1312 (m), 1172 (m), 1073 (m) cm^{-1}; ^1H NMR δ 1.74 (s, 3H, 5-CH_3), 2.54 (dm, *J*=19.6 Hz, 1H, 1-H_n), 2.57 (dm, *J*=18.0 Hz, 1H, 4-H_n), 2.67 (dm, *J*=19.6 Hz, 1H, 3-H_n), 2.85 (dm, *J*=18.4 Hz, 2H, 1-H_x and 3-H_x), 2.98 (s, 3H, *N*–CH_3), 3.08 (dm, *J*=18.0 Hz, 1H, 4-H_x), 5.47 (sext, *J*=1.6 Hz, 1H, 6-H); ^{13}C NMR δ 16.1 (CH_3, C5–CH_3), 25.3 (CH_3, *N*–CH_3), 44.6 (CH_2, C1), 47.9 (CH_2, C4), 48.0 (CH_2, C3), 56.1 (C, C3a), 65.0 (C, C6a), 124.6 (CH, C6), 144.0 (C, C5), 178.9 (C, C7), 180.5 (C, C9), 213.1 (C, C2). HRMS (ESI) (*m*/*z*): calcd for $[C_{12}H_{13}NO_3+H]^+$: 220.0968. Found: 220.0966. Anal. Calcd for $C_{12}H_{13}NO_3$ (219.24): C, 65.74; H, 5.98; N, 6.39. Found: C, 65.77; H, 6.14; N, 6.27.

4.11. X-ray crystal-structure determination of compound 9

A prismatic crystal (0.21×0.367×0.458 mm) was selected and mounted on a D8 Venture diffractometer. Unit-cell parameters were determined from 9908 reflections ($4.07<\theta<72.48°$) and refined by least-squares method. Intensities were collected with graphite monochromatized Cu Kα radiation, using $\omega/2\theta$ scan-technique. 13,737 reflections were measured in the range $5.02\leq\theta\leq72.48$, 2927 of which were non-equivalent by symmetry (R_{int} (on *I*)=0.026). 2653 reflections were assumed as observed applying the condition $I>2\sigma(I)$. Lorentz-polarization and absorption corrections were made. The structure was solved by Direct methods, using SHELXS computer program and refined by full-matrix least-squares method with SHELXLT computer program,[31] using 13,737 reflections (very negative intensities were not assumed). The function minimized was $\Sigma w|F_o|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.0557P)^2+0.5162P]^{-1}$, and $P=(|F_o|^2+2|F_c|^2)/3$, *f*, *f′* and *f″* were taken from International Tables of X-ray Crystallography.[32] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom to which are linked. The final *R* (on *F*) factor was 0.048, *wR*(on $|F|^2$)=0.116 and goodness of fit=1.064 for all observed reflections. Number of refined parameters was 209. Max shift/esd=0.00, mean shift/esd=0.00. Max and min peaks in final difference syntheses were 0.233 and −0.253 e Å^{-3}, respectively (Table 1).

4.12. X-ray crystal-structure determination of compound 10

A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on a Bruker D8 Venture diffractometer. Unit-cell parameters were determined from 1350 reflections ($4.24<\theta<39.23°$) and refined by least-squares method. Intensities were collected with graphite monochromatized Cu Kα radiation, using $\omega/2\theta$ scan-technique. 4516 reflections were measured in the range $4.24\leq\theta\leq39.60$, 922 of which were non-equivalent by symmetry (R_{int} (on *I*)=0.058). 719 reflections were assumed as observed applying the condition $I>2\sigma(I)$. Lorentz-polarization and absorption corrections were made. The structure was solved by Direct methods, using SHELXS computer program and refined by full-matrix least-squares method with SHELX97 computer program,[31] using 4516 reflections (very negative intensities were not assumed). The function minimized was $\Sigma w||F_o|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.0341P)^2+3.3666P]^{-1}$, and $P=(|F_o|^2+2|F_c|^2)/3$, *f*, *f′* and *f″* were taken from International Tables of X-ray Crystallography.[32] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom, which are linked. The final *R* (on *F*) factor was 0.055, *wR* (on $|F|^2$)=0.101 and goodness of fit=1.108 for all observed reflections. Number of refined parameters was 211. Max shift/esd=0.00, mean shift/esd=0.00. Max and min peaks in final difference syntheses were 0.412 and −0.104 e Å^{-3}, respectively. The poor quality of reflections could be due to the fact that the crystal does not diffract very well. Other attempts of crystallization were done, but no single crystals of better quality were obtained (Table 1).

Table 1
Experimental data of the X-ray crystal-structure determination of compounds **9**, **10** and **12**

Compound	**9**	**10**	**12**
Molecular formula	$C_{16}H_{18}N_2O_5$	$C_{16}H_{18}N_2O_5$	$C_{35}H_{37}N_3O_6$
Molecular mass	318.32	318.32	595.68
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/c$	*Pbca*	$P2_1/c$
Cell parameters			
a (Å)	10.9363(3)	12.0636(5)	15.521(5)
b (Å)	10.5601(3	12.4119(5)	25.730(8)
c (Å)	16.0412(4)	20.8539(10)	7.479(3)
α (°)	90	90	90
β (°)	126.2820(10)	90	91.19(2)
γ (°)	90	90	90
V (Å^3)	1493.38(7)	3122.5(2)	2986.1(18)
Z	4	8	4
F(000)	672	1344	1264
d_{calcd} [Mg m^{-3}]	1.416	1.354	1.325
Size of crystal (mm)	0.46×0.37×0.21	0.1×0.09×0.08	0.2×0.09×0.09
Measured reflect.	13,737	4516	25,109
Independent reflect.	2927	922	8306
μ(Mo Kα) (mm^{-1})[a]	0.888	0.850	0.091
μ(Cu Kα) (mm^{-1})[b]			
R	0.044	0.055	0.06
Rw	0.113	0.101	0.151
$\Delta\rho_{max}$[c] (e Å^{-3})	0.233	0.412	0.282
$\Delta\rho_{min}$[d] (e Å^{-3})	−0.253	−0.104	−0.270
Refined parameters	209	211	486
Max shift/esd	0.00	0.00	0.00

[a] μ(Mo Kα) linear absorption coefficient. Radiation Mo Kα (λ=0.71073 Å).
[b] μ(Cu Kα) linear absorption coefficient. Radiation Cu Kα (λ=1.54178 Å).
[c] Maximum peaks in final difference synthesis.
[d] Minimum peaks in final difference synthesis.

4.13. X-ray crystal-structure determination of compound 12

A prismatic crystal (0.1×0.1×0.2 mm) was selected and mounted on a MAR345 diffractometer with an image plate detector. Unit-cell parameters were determined from 208 reflections ($3<\theta<31°$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation. 25,109 reflections were measured in the range $1.31\leq\theta\leq32.40$, 8306 of which were non-equivalent by symmetry (R_{int} (on *I*)=0.076). 6005 reflections were assumed as observed applying the condition $I>2\sigma(I)$. Lorentz-polarization and absorption corrections were made. The structure was solved by Direct methods, using SHELXS computer program,[33] and refined by full-matrix least-squares method with SHELX97 computer program,[33] using 25,109 reflections (very negative intensities were not assumed). The function minimized was $\Sigma w||F_o|^2-|F_c|^2|^2$, where $w=[\sigma^2(I)+(0.0957P)^2]^{-1}$, and $P=(|F_o|^2+2|F_c|^2)/3$, f, f' and f'' were taken from International Tables of X-ray Crystallography.[32] 29H atoms were located from a difference synthesis and refined with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom, which are linked and 8 H atoms were computed and refined using a riding model with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom, which are linked. The final R (on F) factor was 0.086, wR (on $|F|^2$)=0.171 and goodness of fit=1.047 for all observed reflections. Number of refined parameters was 486. Max shift/esd=0.00, mean shift/esd=0.00. Max and min peaks in final difference syntheses were 0.282 and −0.270 e Å^{-3}, respectively.

Acknowledgements

Financial support from Dirección General de Investigación of Ministerio de Economía y Competitividad [project CTQ2011-22433 and fellowship to T.G. (FPI program)] is gratefully acknowledged. M.E.B. thanks the University of Córdoba (Argentina) for financial support. We also thank the *Centres Científics i Tecnològics* of the University of Barcelona (CCiTUB) for NMR, MS and X-ray diffraction facilities, and Ms. P. Domènech from the *Institut de Química Avançada de Catalunya* (IQAC, CSIC, Barcelona, Spain) for carrying out the elemental analyses.

References and notes

1. Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.
2. Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117–7140.
3. Schrodi, Y.; Pederson, R. L. *Aldrichimica Acta* **2007**, *40*, 45–52.
4. Hoveyda, A. H.; Zhugralin, A. R. *Nature* **2007**, *450*, 243–251.
5. Boeda, F.; Clavier, H.; Nolan, S. P. *Chem. Commun.* **2008**, 2726–2740.
6. Samojlowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708–3742.
7. Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746–1787.
8. Nolan, S. P.; Clavier, H. *Chem. Soc. Rev.* **2010**, *39*, 3305–3316.
9. Kotha, S.; Dipak, M. K. *Tetrahedron* **2012**, *68*, 397–421.
10. Arisawa, M.; Nishida, A.; Nakagawa, M. *J. Organomet. Chem.* **2006**, *691*, 5109–5121.
11. Netscher, T. *J. Organomet. Chem.* **2006**, *691*, 5155–5162.
12. Collins, S. K. *J. Organomet. Chem.* **2006**, *691*, 5122–5128.
13. Hassan, H. M. A. *Chem. Commun.* **2010**, *46*, 9100–9106.
14. Kotha, S.; Krishna, N. G.; Halder, S.; Misra, S. *Org. Biomol. Chem.* **2011**, *9*, 5597–5624.
15. Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589–1592.
16. Flynn, A. B.; Ogilvie, W. W. *Chem. Rev.* **2007**, *107*, 4698–4745.
17. Rost, D.; Porta, M.; Gessler, S.; Blechert, S. *Tetrahedron Lett.* **2008**, *49*, 5968–5971.
18. Vorfalt, T.; Leuthäusser, S.; Plenio, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 5191–5194.
19. Kuhn, K. M.; Champagne, T. M.; Hong, S. H.; Wei, W.-H.; Nickel, A.; Lee, C. W.; Virgil, S. C.; Grubss, R. H.; Pederson, R. L. *Org. Lett.* **2010**, *12*, 984–987.
20. Stenne, B.; Timperio, J.; Savoie, J.; Dudding, T.; Collins, S. K. *Org. Lett.* **2010**, *12*, 2032–2035.
21. Sashuk, V.; Peeck, L. H.; Plenio, H. *Chem.—Eur. J.* **2010**, *16*, 3983–3993.
22. Liang, Y.; Raju, R.; Le, T.; Taylor, C. D.; Howell, A. R. *Tetrahedron Lett.* **2009**, *50*, 1020–1022.
23. Paek, S.-M. *Molecules* **2012**, *17*, 3348–3358.
24. Camps, P.; Fernández, J. A.; Rull, J.; Vázquez, S. *Eur. J. Org. Chem.* **2009**, 3081–3087.
25. Vázquez, S.; Camps, P. *Tetrahedron* **2005**, *61*, 5147–5208 and references therein cited.
26. Camps, P.; Muñoz, M. R.; Vázquez, S. *J. Org. Chem.* **2005**, *70*, 1945–1948.
27. Camps, P.; Muñoz, M. R.; Vázquez, S. *Tetrahedron* **2006**, *62*, 7645–7652.
28. Camps, P.; Colet, G.; Delgado, S.; Muñoz, M. R.; Pericàs, M. A.; Solà, L.; Vázquez, S. *Tetrahedron* **2007**, *63*, 4669–4679.
29. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 939628(**9**), CCDC 939904 (**10**), CCDC 939905 (**12**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033]
30. Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160–17161.
31. Sheldrick, G. M. *A Program for Automatic Solution of Crystal Structure Refinement.* Acta Crystallogr.; University of Göttingen: Göttingen, Germany, 2008; Vol. A64, pp 112–221.
32. *International Tables of X-ray Crystallography*; Kynoch: Birmingham, UK, 1974; Vol. IV, pp 99–100 and p 149.
33. Sheldrick, G. M. *SHELX-97: A Computer Program for Crystal Structure Refinement*; University of Göttingen: Germany, 1997.