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High pressure Diels–Alder reactions of (+)-nopadiene with cycloalkenones

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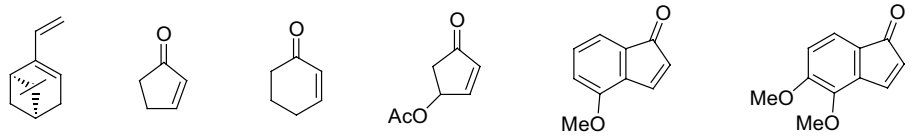
Abstract—Cycloadditions between (+)-nopadiene and 2-cyclopenten-1-one, 2-cyclohexen-1-one, 4-oxo-2-cyclopentenyl-acetate and two indenone derivatives, prepared in situ from the corresponding bromoindanones, have been studied. All cycloadditions are regioselective and *endo-anti* diastereoselective. The best yields were obtained when the Diels–Alder reactions were carried out under high pressure conditions. All new compounds were characterized by their spectroscopic data, in particular by extensive NMR investigations.

1. Introduction

The Diels–Alder (DA) reaction between cycloalkenones and dienes is a powerful method for constructing polycyclic molecules. Cycloalkenones are known to be poorly reactive dienophiles and their DA reactions need to be activated.[1] Herein we report the results of a study on high pressure cycloadditions of (+)-nopadiene **1**, a diene easily available from the chiral pool,[2] with cycloalkenones **2**–**6** (Scheme 1). Inner-outer diene **1** is poorly reactive and, therefore, the Diels–Alder reactions with cycloalkenones have to be accelerated by high pressure[1b,3] and/or by Lewis acid catalysis using mild catalysts because of the sensitivity of diene **1** to acidic conditions. DA reactions of (+)-nopadiene **1** with strong dienophiles that is, phenyl vinyl sulfone,[4] 4-methyl- and 4-phenyl-1,2,4-triazoline-3,5-dione,[5] maleic anhydride,[6] 1,4-benzoquinone, citraconic anhydride and methylacrylate[7] and α-chloroacrylonitrile[8] have been reported. Previously we studied the Diels–Alder cycloadditions of enantiopure cycloalkenones, which are readily available from the chiral pool, (+)-apoverbenone[9] and (+)-carenones,[10] with reactive open chain dienes, in order to open a route to tricyclic compounds, which could be used as intermediates in the synthesis of sesquiterpenes.

Herein we demonstrate that (+)-nopadiene **1** can be used conveniently in [4 + 2]-cycloadditions with cycloalkenones **2**–**6** to prepare, regioselectively and diastereoselectively, polycyclic compounds, which are of interest in the synthesis of chiral nonracemic helical molecules and of optically active tricarbocyclic diterpenes.



1 **2** **3** **4** **5** **6**

Scheme 1.

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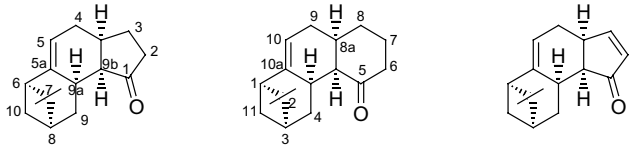
2. Results and discussion

(+)-Nopadiene **1** was prepared according to a previous procedure[2a] using butyl lithium instead of phenyl lithium. The DA cycloadditions were carried out under high pressure conditions and at atmospheric pressure in the presence of a mild Lewis acid catalyst, Et_2AlCl. The optimal results obtained from the many experiments carried out under a variety of conditions are summarized in Tables 1 and 2 and the reaction products reported in Schemes 2 and 3.

Table 2. DA reactions of (+)-nopadiene **1** with indenones **5** and **6** generated in situ from the corresponding bromoindanones **10**

Reactants[a]	Conditions[b]	Product	Yield[c] (%)
1–**5**	1 bar, Et_3N, rfx, 24 h	**11**	19
1–**5**	7 kbar, Et_3N, 35 °C, 18 h	**11**	47
1–**5**	9 kbar, Et_3N, rt, 18 h	**11**	62
1–**6**	1 bar, Et_3N, rfx, 24 h	**12**	22
1–**6**	7 kbar, Et_3N, 35 °C, 18 h	**12**	44
1–**6**	9 kbar, Et_3N, 35 °C, 18 h	**12**	49

[a] Reactant ratio: 1.1:1.
[b] Solvent: CCl_4.
[c] Isolated yield.



7 **8** **9**

Scheme 2.

The DA cycloadditions between (+)-nopadiene **1** and 2-cyclopenten-1-one **2** were carried out at atmospheric pressure and under high pressure in the presence of Et_2AlCl with only cycloadduct **7** (Scheme 2) being obtained regioselectively and *anti*-(with respect to the *gem*-dimethylcyclobutane ring) *endo* diastereoselectively. The best yield (67%) was achieved when the reaction was carried out under high pressure, as shown in Table 1.

The DA reaction between (+)-**1** and 2-cyclohexen-1-one **3** showed a similar outcome: only cycloadduct **8** was obtained with the cycloaddition being totally regioselective and *anti-endo* diastereoselective. Again the best yield (64%) was obtained when the cycloaddition was carried out under high pressure in the presence of Et_2AlCl.

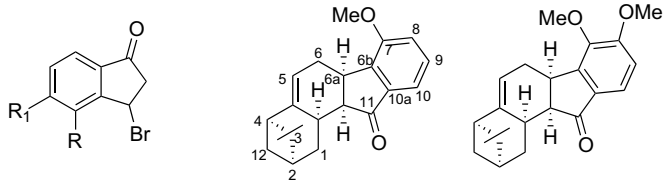
When diene (+)-**1** interacted with 4-oxo-2-cyclopentenyl acetate **4**, at atmospheric pressure under Et_2AlCl catalysis, only tetracyclic α,β-unsaturated ketone **9** (Scheme 2) was obtained in good yield (47%), regioselectively and *anti-endo* diastereoselectively. The best yield (55%) was achieved, however, when the cycloaddition was performed under high pressure (5 kbar) in combination with Et_2AlCl. The formation of tetracyclic conjugated ketone **9** was not surprising since in previous cycloadditions[11] with **4**, cycloadducts underwent ready β-elimination of acetic acid induced by the Lewis acid catalyst or high pressure, thus showing that **4** behaved as a synthetic equivalent of cyclopentadienone.[12]

Two indenones were also included in this study. These dienophiles can be related to cyclopentenones since they allow polycyclic compounds containing a cyclopentenone moiety fused to a benzene ring, to be prepared by DA cycloadditions. The [4 + 2]-cycloadditions were carried out under various conditions, at atmospheric pressure and high pressure with the optimal results summarized in Table 2. Dienophiles **5** and **6** were generated in situ from the bromoketones **10** in the presence of triethylamine.[13,14] Inspection of Table 2 shows the experimental conditions have a profound influence on

Table 1. DA cycloadditions of (+)-nopadiene **1** with cycloalkenones **2**–**4**

Reactants (ratio)	Solvent	Catalyst[a]/ketone	Conditions	Product	Yield[b] (%)
1–**2** (1.5:1)	PhMe	1	1 bar, 25 °C, 4.5 h	**7**	37
1–**2** (0.5:1)	DCM	0.15	4 kbar, 35 °C, 18 h	**7**	67
1–**3** (1.5:1)	PhMe	1	1 bar, 25 °C, 7 h	**8**	29
1–**3** (0.5:1)	DCM	0.15	4 kbar, 35 °C, 18 h	**8**	64
1–**4** (1.2:1)	DCM	1	1 bar, 30 °C, 3 h	**9**	47
1–**4** (1.2:1)	DCM	1	5 kbar, 30 °C, 5 h	**9**	55

[a] Et_2AlCl.
[b] Isolated yield.



10 a, R=OMe, R_1=H
b, R=R_1=OMe **11** **12**

Scheme 3.

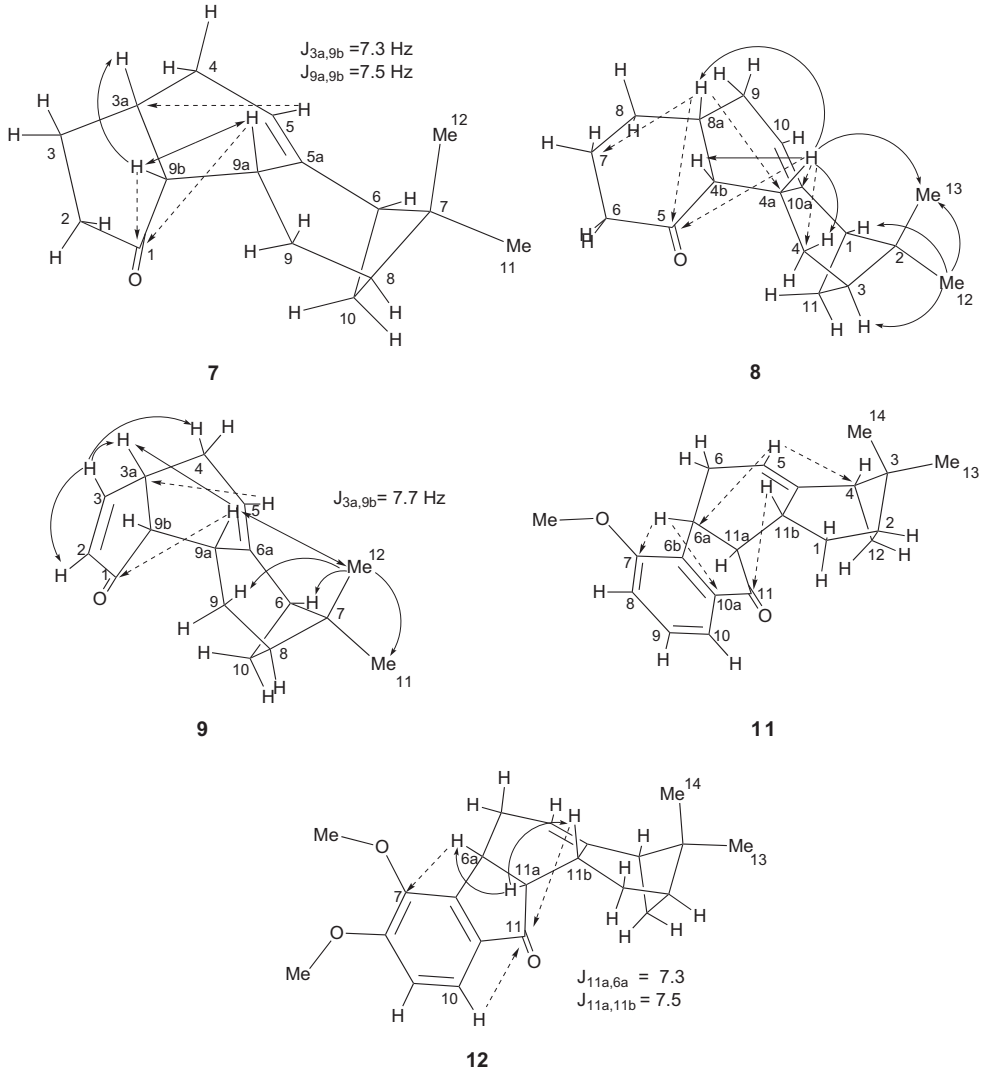


Figure 1. Minimized energy conformations of ketones **7**–**9**, **11** and **12**; the arrows indicate observed NOEs; dotted arrows indicate long-range hetero-correlation.

the outcome of the processes. The best results were obtained when indenones **5** and **6** were treated under high pressure conditions giving 62% and 49%, respectively.

As the data in Table 2 show, the reaction yield depended on the pressure.

These conditions regioselectively and *anti*-(with respect to the *gem*-dimethylcyclobutane ring) *endo*-diastereoselectively produced cycloadducts **11** and **12** (Scheme 3). Drops in yield were observed when the cycloadditions were carried out under thermal conditions.

3. Structural analysis

The structure and the stereochemistry of the products were inferred from the analysis of their high-field ^{1}H and ^{13}C NMR spectra. The ^{1}H and ^{13}C assignments follow from 2D ^{1}H–^{1}H, ^{1}H–^{13}C connectivities (COSY and HETCOR experiments). The pertinent data are collected in the experimental section. The regiochemistry of the carbonyl function was based on the long-range hetero-correlations inferred from 2D INEPT (or HMBC) experiments (see Fig. 1). The stereochemistry at the ring junctions as well as the *cis*-relationship of *gem*-dimethyl group and the hydrogens at the ring junctions, followed from selective NOE experiments (see Fig. 1) and $J_{H,H}$ coupling constant values.

The regiochemistry of the carbonyl functions of **7** and **9** were established by the long-range hetero-correlations observed between H-5 and C-3a and between H-9a and C-1. The all-*cis* arrangements of H-3a, H-9a and H-9b protons were deduced from the NOEs observed among these protons. Furthermore, in the case of **9**, mutual enhancement occurred for resonances of H-9a, H-3a and the methyl group at C-7 ($\delta = 0.78$ ppm), thus indicating the stereochemistry depicted in the formula.

The *cis*-relationship of the 6,8-methane bridge and the ring junction protons for ketone **7** was based on the similarity of their ^{13}C chemical shifts with those of ketone **9**.

Final proof of the stereochemical assignment of both ketones is given by the coupling values, that is, $^3J_{3a,9b} = 7.7$ Hz for **9** and $^3J_{3a,9b} = 7.3$ Hz, $^3J_{9b,9a} = 7.5$ Hz for **7**.

The position of the carbonyl function of **8** was established from the long-range hetero-correlations observed between H-4a and C-5, C-10a and C-4 and between H-8a and C-5, C-7 and C-4a (see Fig. 1). The *cis*-relationship of the 1,3-methane bridge and the ring junction hydrogens follows from the NOEs observed on H-4b, H-8a and the methyl hydrogens at C-2 ($\delta = 0.97$) upon irradiation of H-4a (Fig. 1).The coupling constant values of H-4b ($^2J_{4b,4a} = 4.6$ Hz and $^2J_{4b,8a} = 4.9$ Hz) confirmed the *cis*-relationship between H-4a, H-4b and H-8a. The structure and stereochemistry of cycloadducts **11** and **12** was based, first of all, on the similarity of their ^{13}C chemical shift with those of ketones **7**–**9** discussed above. The regiochemistry of the carbonyl function of **11** and **12** was confirmed from the long-range hetero-correlations observed on C-11 upon selective irradiation of H-11 and on C-7 upon selective irradiation of H-6a for both ketones. Finally, in the case of ketone **12** the NOEs observed on H-6a and H-11b upon selective irradiation of H-11a, as well as the coupling constant values of H-11a ($^3J_{11a,6a} = 7.3$ and $^3J_{11a,11b} = 7.5$ Hz) confirmed the all-*cis* arrangements of these protons (see Fig. 1).

4. Conclusions

DA cycloadditions of (+)-nopadiene **1** with cycloalkenones occurred in good yields when activated by high pressure in combination with Et_2AlCl catalyst. The reactions are totally regioselective and *anti-endo* diastereoselective and provide a new approach to optically active polycyclic compounds in view of the ready availability of nopadiene in each of its enantiomeric forms and a facile conversion of the *gem*-dimethylcyclobutane ring into a variety of substances.

5. Experimental

5.1. General

Melting points were determined on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ solution at rt on a Perkin–Elmer Paragon 500 FT-IR. Mass spectra were observed on a Hewlett–Packard 5970 GC–MS instrument (70 eV). Optical rotations were measured in $CHCl_3$ solution on a Jasco DIP-360 polarimeter in a quartz cell at 25 °C. GC analyses were performed on a Hewlett–Packard 6890 chromatograph. Absorption chromatography was carried out on Riedel de Haën silica gel (32–63 μm; 230–400 mesh ASTM). The NMR spectra were recorded on a Varian Associates VXR-400 multinuclear instrument in $CDCl_3$ solution (internal standard: TMS). ^{1}H and ^{13}C shift assignments were based on COSY, ^{1}H–{^{1}H}NOE and HETCOR experiments.

A commercially available 1 M hexane solution of Et_2AlCl was used; toluene was distilled from Na and $LiAlH_4$; CH_2Cl_2 was distilled from CaH_2. Commercial *N*-bromosuccinimide was freshly crystallized from water before use. Commercial 4-methoxy-indan-1-one and 4,5-dimethoxy-indan-1-one were used to prepare the corresponding bromoindanones **10**. All preparations of starting mixtures were done in a dry box.

5.2. General procedure for the high pressure Diels–Alder reactions of (+)-nopadiene 1 with cycloalkenones 2–4

The following discussion of the **1**–**2** reaction is a typical procedure used for all cycloadditions. Details are listed in Table 1.

A hexane solution (1 M) of Et_2AlCl (0.09 mL, 0.09 mmol) was added to a solution of 2-cyclopenten-1-one **2** (0.05 g, 0.60 mmol) in dry CH_2Cl_2 (2 mL) and the mixture stirred at room temperature for 40 min.[15] A solution of diene **1** (0.045 g, 0.30 mmol) in dry CH_2Cl_2 (1 mL) was then added and the whole mixture placed into a Teflon ampoule. The ampoule was closed and kept under 4 kbar pressure for 18 h at 35 °C. After depressurizing, the mixture was poured into a cooled saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel eluting with 95:5 hexane/ethylacetate to afford cycloadduct **7** (0.046 g, 0.20 mmol, 67%) as a colourless oil; $[\alpha]_D = +16$ (*c* 1.24, $CHCl_3$); IR: 1730 (s, C=O) cm^{-1}; ^{1}H NMR δ 0.84 (s, 3H, Hs-12), 1.11 (s, 1H, $J = 10.2$ Hz, H-10), 1.26 (s, 3H, Hs-11), 1.67 (ddd, 1H, $J = 12.8$, 7.9, 4.0 Hz, H-3), 1.92 (ddd, 1H, $J = 16.7$, 5.7, 4.0 Hz, H-2), 2.00 (m, 2H, H-8, H-9), 2.01 (m, 1H, H-2), 2.02 (m, 1H, H-4), 2.14 (dd, 1H, $J = 10.2$, 8.4 Hz, H-10), 2.15 (ddd, 1H, $J = 12.8$, 9.6, 3.6 Hz, H-3), 2.32 (ddd, 1H, $J = 14.3$, 8.4, 2.9 Hz, H-4), 2.32 (m, 1H, H-6), 2.42 (ddd, 1H, $J = 8.4$, 6.4, 1.3 Hz, H-9b), 2.61 (ddd, 1H, $J = 14.3$, 3.5, 2.3 Hz, H-9), 2.75 (m, 1H, H-9a), 2.78 (m, 1H, H-3a), 5.32 (ddd,1H, $J = 5.9$, 3.1, 2.9 Hz, H-5); ^{13}C NMR δ 22.6 (C-12), 26.7 (C-11), 26.8 (C-9), 29.0 (C-3), 29.1 (C-4), 31.0 (C-10), 32.4(C-9a), 35.2 (C-3a), 39.2 (C-2), 40.7 (C-7), 42.1 (C-8), 50.7 (C-6), 51.5 (C-9b), 117.6 (C-5), 146.6 (C-5a), 221.5 (C-1); MS, *m*/*z* (rel. intensity) 43 (4), 55 (9), 69 (8), 83 (base), 91 (28), 105 (32), 117 (54), 133 (16), 148 (31), 158 (2), 169 (30), 187 (16), 197 (3), 212 (13), 230 (M^+, 3). Anal. Calcd for $C_{16}H_{22}O$: C,83.43; H, 9.63. Found: C, 83.40; H, 9.64%.

5.3. General procedure for the Et_2AlCl-catalyzed Diels–Alder reactions of (+)-nopadiene 1 with cycloalkenones 2–4

The following discussion of the **1**–**2** reaction is a typical procedure used for all cycloadditions. Details are listed in Table 1.

To a solution of ketone **2** (0.12 g, 1.46 mmol) in 7 mL of dry toluene were added 1.46 mL (1.46 mmol) of a 1 M hexane solution of Et_2AlCl and the mixture stirred at

room temperature for 40 min. A solution of 0.33 g (2.23 mmol) of nopadiene **1** in dry toluene (8 mL) was then added and the reaction mixture kept under stirring at 25 °C for 4.5 h. It was cooled and then poured into a saturated $NaHCO_3$ solution. The organic layer was then washed with saturated brine, dried over Na_2SO_4 and evaporated under reduced pressure to give the crude adduct **7**, which was chromatographed on silica gel and eluted with 95:5 hexane/ethyl acetate to produce 0.12 g (0.54 mmol, 37%) of pure cycloadduct **7**.

Cycloadduct ***8***: purified by column chromatography on silica gel eluting with hexane/ethylacetate 95:5; mp 89–90° (methanol); $[\alpha]_D = -74$ (*c* 0.21, $CHCl_3$); IR: 1709 (s, C=O) cm^{-1}; ^1H NMR δ 0.97 (s, 3H, Hs-13), 1.28 (s, 3H, Hs-12), 1.68 (ddd, 1H, $J = 13.4$, 4.2, 2.4 Hz, H-8), 1.94 (ddd, 1H, $J = 12.6$, 10.8, 3.8 Hz, H-4), 1.95–2.02 (m, 5H, H-4, Hs-7, H-8, H-9), 2.04 (ddd, 1H, $J = 12.6$, 7.7, 2.2 Hz, H-9), 2.05 (m, 2H, H-3, H-11), 2.28 (m, 1H, H-6), 2.38 (m, 1H, H-6), 2.42 (m, 1H, H-11), 2.43 (m, 1H, H-1), 2.65 (m, 1H, H-8a), 2.75 (ddd, 1H, $J = 7.7$, 4.9, 4.6 Hz, H-4a), 2.83 (dd, 1H, $J = 4.9$, 4.6 Hz, H-4b), 5.08 (m, 1H, H-10); ^{13}C NMR δ 23.2 (C-13), 24.4 (C-7), 27.3 (C-9), 27.7 (C-12), 29.6 (C-4), 30.4 (C-8), 32.8 (C-11), 34.0 (C-4a), 40.2 (C-2), 40.4 (C-8a), 42.7 (C-3), 43.5 (C-6), 52.4 (C-1), 52.9 (C-4b), 114.7)C-10), 143.5 (C-10a), 211.5 (C-5); MS, *m/z* (rel. intensity) 43 (6), 55 (7), 69 (6), 79 (11), 97 (base), 106 (3), 117 (17), 133 (16), 148 (17), 157 (9), 173 (3), 183 (15), 201 (6), 211 (3), 226 (9), 244 (M^+, 10). Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.50; H, 9.92%.

Tetracyclic ketone ***9***: purified by column chromatography on silica gel eluting with hexane/ethylacetate 95:5; colourless oil; $[\alpha]_D = +38$ (*c* 0.95, $CHCl_3$); IR: 1693 (s, C=O) cm^{-1}; ^1H NMR δ 0.78 (s, 3H, Hs-12), 0.94 (m, 1H, H-10), 1.22 (s, 3H, Hs-11), 2.05 (m, 2H, H-8, H-9), 2.18 (m, 1H, H-10), 2.21 (m, 1H, H-4), 2.28 (m, 1H, H-6), 2.61 (dd, 1H, $J = 7.7$, 5.9 Hz, H-9b), 2.68 (m, 1H, H-9a), 2.91 (ddd, 1H, $J = 13.4$, 4.4, 3.0 Hz, H-9), 3.29 (ddd, 1H, $J = 7.7$, 2.4, 2.0 Hz, H-3a), 5.21 (ddd, 1H, $J = 5.9$, 4.6, 2.8 Hz, H-5), 6.16 (dd, 1H, $J = 5.6$, 2.0 Hz, H-2); ^{13}C NMR δ 22.3 (C-12), 24.6 (C-9), 26.0 (C-4), 26.2 (C-11), 29.7 (C-10), 33.3 (C-9a), 40.9 (C-7), 42.1 (C-8), 43.0 (C-3a), 48.4 (C-9b), 49.6 (C-6), 115.3 (C-5), 137 (C-2), 147.1 (C-5a), 167.7 (C-3), 212.4 (C-1); MS, *m/z* (rel. intensity) 55 (20), 69 (9), 82 (33), 91 (66), 105 (base), 115 (19), 131 (23), 147 (37), 167 (6), 185 (36), 210 (6), 228 (M^+, 6). Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.17; H, 8.84%.

5.4. General procedure for high pressure Diels–Alder reactions of (+)-nopadiene 1 with indenones 5 and 6 generated in situ

Details are listed in Table 2.

Bromoindanones **10** were prepared by NBS bromination of indanones.[13,14] The following discussion of the **1**–**5** reaction is the procedure used for the cycloaddition between **1** and **6** too.

Details are listed in Table 2.

A solution of bromoindanone **10a** (0.48 g, 1.99 mmol) in CCl_4 (8 mL) was added to triethylamine (0.30 g, 2.97 mmol) and a solution of diene **1** (0.30 g, 2.03 mmol) in CCl_4 (7 mL) and kept at 9 kbar at room temperature for 18 h. The reaction was then worked-up as usual to give a crude product that was purified by column chromatography on silica gel eluting with hexane/ethyl acetate 90:10 to give pure **11** (0.38 g, 1.23 mmol, 62%); $[\alpha]_D = -180$ (*c* 0.86, $CHCl_3$); IR: 1699 (s, C=O) cm^{-1}; ^1H NMR δ 0.80 (s, 3H, Hs-14), 1.10 (d, 1H, $J = 9.3$ Hz, H-12), 1.21 (s, 3H, Hs-13), 2.05 (dddd, 1H, $J = 7.4$, 3.2, 3.0, 2.7 Hz, H-2), 2.12 (ddd, 1H, $J = 13.7$, 10.7, 3.0 Hz, H-1), 2.20 (m, 2H, H-4, H-12), 2.22 (m, 1H, H-6), 2.79 (ddd, 1H, $J = 10.7$, 7.4, 4.6 Hz, H-11b), 2.88 (ddd, 1H, $J = 14.9$, 7.3, 1.5 Hz, H-6), 2.89 (dd, 1H, $J = 7.4$, 7.2 Hz, H-11a), 3.08 (ddd, 1H, $J = 13.7$, 4.6, 3.2 Hz, H-1), 3.81 (ddd, 1H, $J = 7.3$, 7.2, 1.5 Hz, H-6a), 3.91 (s, 3H, OMe), 7.01 (dd, 1H, $J = 7.6$, 1.5 Hz, H-8), 7.24 (dd, 1H, $J = 7.6$, 1.5 Hz, H-10), 7.29 (d, 1H, $J = 7.6$ Hz, H-9), 5.09 (dd, 1H, $J = 7.3$, 2.9 Hz, H-5); ^{13}C NMR δ 22.4 (C-14), 25.3 (C-1), 25.5 (C-6), 26.3 (C-13), 29.5 (C-12), 33.6 (C-11b), 38.0 (C-6a), 41.1 (C-3), 42.1 (C-2), 49.5 (C-4), 50.5 (C-11a), 55.6 (OMe), 114.7 (C-10), 115.5 (C-8), 116.6 (C-5), 129.0 (C-9), 141.4 (C-10a), 145.8 (C-7), 147.9 (C-4a), 157.3 (C-6b), 209.5 (C-11); MS, *m/z* (rel. intensity) 43 (9), 77 (11), 91 (33), 105 (49), 131 (20), 147 (41), 162 (base), 178 (10), 221 (18), 247 (23), 265 (68), 290 (21), 308 (M^+, 8). Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.80; H, 7.85%.

5.5. Thermal reactions of (+)-nopadiene 1 with indenones 5 and 6 generated in situ

Details are listed in Table 2.

To a solution of bromoindanone **10a** (0.16 g, 0.66 mmol) in CCl_4 (6 mL) was added a solution of diene **1** (0.10 g, 0.67 mmol) in CCl_4, 0.10 g (0.99 mmol) of triethylamine and a few crystals of hydroquinone. The reaction mixture was heated at reflux temperature for 24 h, then worked-up as usual. After removal of the solvent in vacuo the crude cycloadduct **11** was purified by column chromatography on silica gel with hexane/ethyl acetate 90:10.

Pentacyclic ketone ***12***: purified by column chromatography on silica gel with hexane/ethyl acetate 90:10; $[\alpha]_D = -111$ (*c* 0.60, $CHCl_3$); IR: 1683 (s, C=O) cm^{-1}; ^1H NMR δ 0.79 (s, 3H, Hs-14), 1.05 (d, 1H, $J = 9.3$ Hz, H-12), 1.21 (s, 3H, Hs-13), 2.02 (m, 1H, H-2), 2.12 (ddd, 1H, $J = 313.7$, 10.8, 3.0 Hz, H-1), 2.20 (m, 2H, H-4, H-12), 2.28 (m, 1H, H-6), 2.77 (ddd, 1H, $J = 10.8$, 7.5, 4.5 Hz, H-11b), 2.86 (ddd, 1H, $J = 14.9$, 7.1, 1.4 Hz, H-6), 2.91 (dd, 1H, $J = 7.5$, 7.3 Hz, H-11a), 3.08 (ddd, 1H, $J = 13.7$, 4.5, 3.2 Hz, H-1), 3.82 (ddd, 1H, $J = 7.3$, 7.1, 1.3 Hz, H-6a), 3.93 (s, 3H, 7-OMe), 3.93 (s, 3H, 8-OMe), 5.13 (ddd, 1H, $J = 6.9$, 3.0, 2.9 Hz, H-5), 6.93 (d, 1H, $J = 8.6$ Hz, H-9), 7.40 (d, 1H, $J = 8.6$ Hz, H-10); ^{13}C NMR δ 22.4 (C-14), 25.0 (C-1), 26.1 (C-6), 26.2 (C-13), 29.6 (C-12), 33.6 (C-11b), 38.0

(C-6a), 41.0 (C-3), 42.0 (C-2), 49.5 (C-4), 50.8 (C-11a), 56.4 (8-OMe), 60.6 (7-OMe), 112.6 (C-9), 116.6 (C-5), 119.4 (C-10), 134.1 (C-10a), 145.8 (C-7), 148.0 (C-4a), 150.0 (C-6b), 158.1 (C-8), 207.7 (C-11); MS, *m*/*z* (rel. intensity) 43 (5), 77 (5), 91 (13), 105 (19), 147 (16), 177 (20), 191 (base), 251 (8), 295 (26), 320 (12), 338 (M^+, 9). Anal. Calcd for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74. Found: C, 78.10; H, 7.73%.

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