Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 5477–5481

High pressure and thermal Diels–Alder reactions of 5-nitro[2.2]paracyclophanepyran-6-one

Lucio Minuti,[a,*] Assunta Marrocchi,[a] Selvaggia Landi,[a] Mirko Seri[a] and Eszter Gacs-Baitz[b]

[a]*Dipartimento di Chimica, Università degli Studi di Perugia, via Elce di Sotto 8, 06123 Perugia, Italy*
[b]*Central Institute for Chemistry, Hungarian Academy of Sciences, PO Box 17, H-1525 Budapest, Hungary*

Received 22 January 2007; revised 26 March 2007; accepted 12 April 2007
Available online 20 April 2007

Abstract—The Diels–Alder reactions of 5-nitro[2.2]paracyclophanepyran-6-one with 1,3-butadienes and 1,2-dihydro-3-vinyl-naphthalene were examined under thermal and high-pressure conditions. The cycloadditions with 1,3-butadienes occurred in good yield and *anti-exo* diastereoselectively only under high-pressure conditions; the one with 1,2-dihydro-3-vinyl-naphthalene afforded comparable yields of mixtures of *anti*/*syn* adducts under normal and high-pressure conditions. A structural analysis of the reaction products by ^{1}H and ^{13}C NMR spectroscopy is presented.

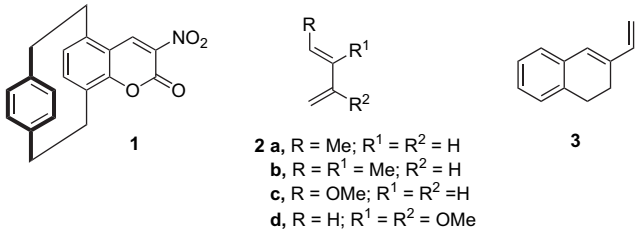
1. Introduction

In a recent paper[1] from this laboratory we have described the preparation of 5-nitro[2.2]paracyclophanepyran-6-one **1**, a new example of a coumarin derivative incorporating a [2.2]paracyclophane unit, and we showed that the cycloaddition of 1,3-butadienes to **1** provides an easy entry to angularly fused polycyclic [2.2]paracyclophanes containing heterocyclic rings. These compounds are of interest due to their optical and electronic properties and their potential applications in the field of material science.[2]

In view of our increasing interest in planar and helical polycyclic [2.2]paracyclophanes,[3] we have extended the study of the Diels–Alder reaction of nitrocoumarin **1** to open-chain and exocyclic-vinyl ring dienes in order to investigate the possibility of accessing new structurally diverse multi-ring heterocyclic systems.

The coumarins are poorly reactive dienophiles and, therefore, their [4+2]cycloaddition reactions with dienes need to be activated.[1,4] In the case of coumarin **1**, despite activation by a strong electron-withdrawing nitro group, the use of strong Lewis acids is limited in light of the sensitivity of the coumarinic skeleton to acidic conditions. The use of very high reaction temperatures is also precluded due to the heat sensitivity of the [2.2]paracyclophane unit,[5] so the reactions have to be accelerated by high pressure.[6]

Herein, we report the high pressure and thermal Diels–Alder reaction of coumarin **1** with 1,3-butadienes **2a–d** and the exocyclic-vinyl ring diene **3** (Scheme 1); the latter being particularly useful for checking the possibility of opening up a route to extended helical cyclophanes.[7]



Scheme 1.

We also present a systematic ^{1}H and ^{13}C NMR spectroscopic investigation of the cycloadducts from the viewpoint of structural and stereochemical assignments.

2. Results and discussion

5-Nitro[2.2]paracyclophanepyran-6-one (**1**) was prepared according to a previously reported procedure.[1]

The Diels–Alder cycloadditions between **1** and dienes **2a–d** and **3** were examined under different experimental conditions, under both high pressure and atmospheric pressure. The optimal results are summarized in Table 1 and the reaction products are reported in Scheme 2.

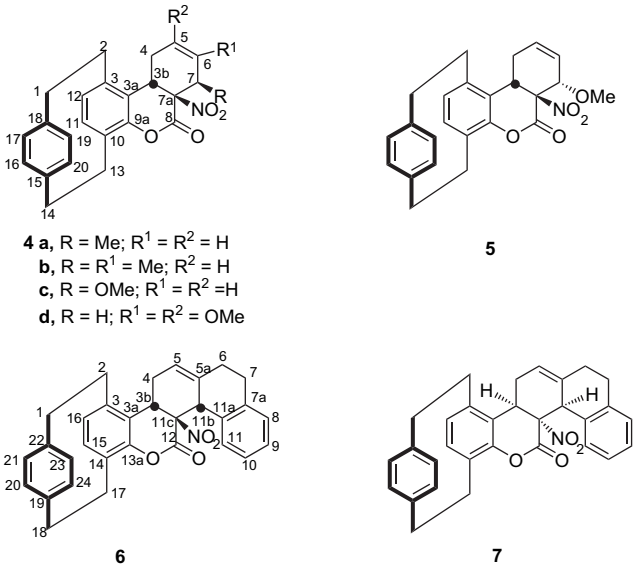
Keywords: [2.2]Paracyclophanes; Coumarins; High pressure; Diels–Alder cycloaddition.
* Corresponding author. Tel.: +39 075 5855545; fax: +39 075 5855560; e-mail: lucio@unipg.it

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.04.042

Table 1. Diels–Alder reactions of 5-nitro[2.2]paracyclophanepyran-6-one (**1**) with dienes **2a–d** and **3** under normal- and high-pressure conditions

Diene (equiv)	Conditions	Products (ratio)	Yield[a] (%)
2a (4)	8 kbar, CH_2Cl_2, 50 °C, 20 h	**4a**	53
2a (6)	Toluene, 110 °C, 39 h	—	—
2b (4)	8 kbar, CH_2Cl_2, 50 °C, 24 h	**4b**	64
2b (4)	Toluene, 110 °C, 39 h	**4b**	33
2c (2)	8 kbar, CH_2Cl_2, 35 °C, 24 h	**4c**, **5** (1:1.8)	69
2c (2)	Toluene, 110 °C, 24 h	**4c**, **5** (1:2)	42
2d (4)	8 kbar, CH_2Cl_2, 50 °C, 20 h	**4d**	98
2d (6)	Toluene, 110 °C, 24 h	**4d**	67
3 (2)	8 kbar, CH_2Cl_2, 50 °C, 24 h	**6**, **7** (18:1)	70
3 (4)	Toluene, 110 °C, 40 h	**6**, **7** (2:1)	75

[a] Yields of isolated cycloadducts.



Scheme 2.

When compound **1** interacted with (*E*)-piperylene (**2a**) under normal pressure conditions in toluene solution at 110 °C, no reaction occurred, although a variety of conditions were tested. The Diels–Alder reaction occurred only under high-pressure conditions (8 kbar) and gave, regioselectively and *anti*-(with respect to the unsubstituted arene ring of the paracyclophane unit)-*exo* diastereoselectively, the cycloadduct **4a** in good yield (53%) (Table 1).

The Diels–Alder reaction between **1** and 2-methyl-1,3-pentadiene **2b** showed a similar outcome: only cycloadduct **4b** was obtained, with the cycloaddition again being totally regioselective and *anti-exo* diastereoselective. In this case, diene **2b** also reacted at atmospheric pressure confirming higher reactivity with respect to **2a**, although with modest yield (33%). The best yield (64%) was once again achieved when the cycloaddition was performed under hyperbar activation (8 kbar).

The *anti* diastereoselectivity observed in the cycloadditions of dienes **2a** and **2b** was expected[1,3] and may be ascribed to the severe non-bonding interactions between the arene ring and the dienes in the transition state for the *syn* addition; on the other hand, the exclusive *exo* addition is quite surprising, since the *endo* addition is generally considered the preferred reaction path of the Diels–Alder reaction, on the basis of secondary orbital interactions stabilizing the *endo* transition state[8] and/or under high-pressure conditions.[6] The observed *exo* preference may be the consequence of an *exo* transition state incorporating a prevalent stabilizing, secondary orbital interaction between the diene and nitro group.[4d]

To further evaluate the reactivity and the regio- and diastereoselectivity at normal and high pressures, we extended the study to the Diels–Alder reaction of nitrocoumarin **1** with two alkoxy-dienes: (*E*)-1-methoxy-1,3-butadiene (**2c**) and 2,3-dimethoxy-1,3-butadiene **2d** (Table 1).

At atmospheric pressure, the cycloaddition of **2c** and **2d** occurred at 110 °C in 42% and 67% yield, respectively; better yields (69% for **2c** and 98% for **2d**) were achieved once again when the reactions were carried out under high pressure (Table 1). As expected, the cycloadditions were always totally *anti*-(with respect to the unsubstituted arene ring of the paracyclophane unit) diastereoselective, affording adduct **4d** with 2,3-dimethoxy-1,3-butadiene (**2d**) and a mixture of adducts **4c/5** with (*E*)-1-methoxy-1,3-butadiene (**2c**). As shown by the structural assignment, the cycloadducts **4c** and **5** were the *exo*/*endo* adducts. Whereas the reactions of dienes **2a** and **2b** were totally *exo* diastereoselective, as reported above, the reaction of diene **2c** led to a slight prevalence of *endo* adduct when carried out at atmospheric pressure (*endo*/*exo*=2:1) and at 8 kbar (*endo*/*exo*=1.8:1). The low *endo*/*exo* diastereoselectivity of the reaction of (*E*)-1-methoxy-1,3-butadiene (**2c**) may be the consequence of a comparable, stabilizing secondary orbital interaction originating between 1,3-diene and the carbonyl group in the *endo* approach and between the 1,3-diene and the nitro group in the *exo* transition state.

Finally, in order to gain some information about the parameters controlling the regiochemistry and to check the possibility of opening up a route to helical cyclophanes containing heterocyclic rings, we also examined the Diels–Alder reaction of **1** with 1,2-dihydro-3-vinyl-naphthalene (**3**), an exocyclic-vinyl ring diene previously prepared in our laboratory[9] and used to synthesize pentahelicenes[9,7a] (Scheme 1). As shown in Table 1, the reaction of **1** with diene **3** occurred in satisfactory yields at normal pressure (75%) as well as under hyperbar activation (70%) leading regioselectively and *endo* diastereoselectively to a mixture of the *anti*/*syn* (with respect to the unsubstituted arene ring of the paracyclophane unit) adducts **6/7**. Whereas the cycloaddition under high pressure was highly *anti* diastereoselective (**6/7**= 18/1), the NMR structural assignment surprisingly shows that the cycloaddition at normal pressure gave only a slight prevalence of *anti* adduct (**6/7**=2/1). The formation of the *endo-syn* adduct **7** under thermal condition was unexpected and inexplicable in view of the severe destabilizing non-bonding interactions between the unsubstituted arene ring of [2.2]paracyclophane and the diene in the *endo-syn* approach.

3. Structural analysis

The structure and stereochemistry of the products were assigned by analyzing the ^1H and ^{13}C NMR spectra. Proton

and carbon shift assignments follow from the examination of ^1H–^1H and ^1H–^{13}C connectivities (COSY and HETCOR spectra); quaternary carbons were assigned by 2D long-range hetero-correlated experiments. The pertinent data are given in Section 5. The stereochemical assignments were based on J_{HH} coupling constant values and selective ^1H–{^1H} NOEs.

Selective pre-irradiation of the resonance due to H-3b in compounds **4a–d** and **5** resulted in signal enhancements of the resonance attributed to H-19. This indicated that H-3b points toward the unsubstituted arene ring of the paracyclophane unit, confirming a total *anti* diastereoselectivity in the cycloaddition reactions between **1** and 1,3-butadienes **2a–d**. Furthermore, the NOEs observed between H-3b and the C-7 methyl protons for compounds **4a** and **4b** revealed a cis-relationship between the methyl group at C-7 and H-3b for both compounds. Support for the latter assignment was given when similar chemical shifts for the C-7 and C-7a carbons were observed in the two compounds (33.5 and 32.7 for C-7, 92.4 and 92.9 for C-7a in **4a** and **4b**, respectively), thus confirming a total *anti-exo* diastereoselectivity in the cycloaddition reactions.

The configuration of the methoxy group at C-7 in compounds **4c** and **5** was derived from the NOE experiments. Whereas irradiation of the resonance due to H-7 resulted in signal enhancement of the resonances attributed to H-3b, H-4, H-6, and the methoxy group protons in compound **5**, in compound **4c** NOEs were observed only between H-7, H-6, and the methoxy group protons, thus revealing a cis- and trans-relationship between the methoxy group and H-3b for **4c** and **5**, respectively.

Finally, the structure of compounds **6** and **7** was assigned. The long-range coupling observed between H-11b and H-4, H-5, and H-6, as well as the absence of coupling between H-3b and H-11b protons, indicated the structure assigned to **6** and **7**, thus confirming a total regioselectivity in the cycloaddition reaction. The stereochemical assignment was inferred from a series of selective NOE experiments. Selective irradiation of the resonance due to H-3b in compound **6** resulted in signal enhancements of the resonances attributed to H-2, H-11b, and H-23. These results unambiguously indicate a cis-relationship between H-3b and H-11b and that both these protons point toward the unsubstituted arene ring of the paracyclophane unit. In contrast, when the same experiment was performed with compound **7**, strong signal enhancement was only observed for H-11b. This observation pointed out an opposite configuration of both H-3b and H-11b with respect to the unsubstituted arene ring of the paracyclophane unit, as depicted in the formula (Scheme 2). The assignment of the structure to **7** was also supported by the high-field shift of one of the C-4 protons (1.62 ppm), which reflects its proximity to the aromatic ring of the paracyclophane unit.

4. Conclusion

Diels–Alder reactions of 5-nitro[2.2]paracyclophanepyran-6-one **1** with various 1,3-butadienes and an exocyclic-vinyl ring diene were examined under thermal and high-pressure conditions. The cycloadditions occurred in good yields when activated by high pressure, in the case of the reaction of **1** with the less reactive (*E*)-piperylene **2a**, pressure had to be applied in order for the reaction to occur. All the cycloadditions of **1** with **2a–d** were totally regioselective and *anti-exo* diastereoselective, except the reaction of **1** with **2c**, which produced a mixture of *exo*/*endo* adducts; in contrast the reaction of **1** with **3** was totally *endo* diastereoselective and highly *anti* diastereoselective.

The reactions provide a new synthetic route to multi-ring [2.2]paracyclophanepyranones and also to [2.2]paracyclophanes bearing a condensed benzofuran subunit in view of the previously reported conversion of the nitrotetrahydrobenzochromene unit into benzofurans by Nef-cyclodehydration reactions.[1]

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 FTIR.

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). ^1H and ^{13}C NMR shift assignments were based on COSY, ^1H–{^1H} NOE, and HETCOR experiments.

5.2. General procedure for the Diels–Alder reaction of 5-nitro[2.2]paracyclophanepyran-6-one (1) with dienes 2a–d and 3

The cycloadditions of **1** with dienes **2a–d** and **3** were accomplished (A) under high-pressure conditions and (B) under normal pressure. The following discussion of the reaction of **1** with **2a** is a typical procedure used for all cycloadditions. Details are listed in Table 1.

Conditions (A): a solution of compound **1** (0.48 g, 1.5 mmol) and diene **2a** (6 mmol) in 10 ml of CH_2Cl_2 in the presence of a few crystals of hydroquinone was placed in a 15 ml Teflon vial that was then filled with CH_2Cl_2. The vial was closed and kept at 8 kbar at 50 °C for 20 h. After depressurizing, the solvent was removed in vacuo. The crude mixture obtained was purified by column chromatography on silica gel followed by recrystallization.

Conditions (B): a solution of **1** (0.16 g, 0.5 mmol) and diene **2a** (3 mmol) in toluene (5 ml) was heated in an oil bath at 110 °C for 39 h. After cooling, the solvent was evaporated in vacuo and the residue purified by column chromatography on silica gel followed by recrystallization.

5.2.1. Compound 4a. Purified by column chromatography eluting with 4:1 hexane/EtOAc; mp 197–198 °C (hexane/EtOAc); IR: 2342 (s, C–N), 1770 (s, C=O), 1557 (C–NO_2) cm^{-1}; ^1H NMR δ 1.45 (d, 3H, J=7.3 Hz, Me), 1.80

(ddd, 1H, *J*=19.1, 7.9, 2.9 Hz, H-4), 2.42 (ddd, 1H, *J*=19.1, 7.5, 4.7 Hz, H-4), 2.76 (ddd, 1H, *J*=13.9, 10.8, 3.8 Hz, H-13), 2.97–3.26 (m, 6H, H-1, H-2, H-14), 3.36 (dd, 1H, *J*=7.3, 4.1 Hz, H-7), 3.38 (ddd, 1H, *J*=13.9, 10.6, 4.1 Hz, H-13), 4.06 (dd, 1H, *J*=7.9, 7.5 Hz, H-3b), 5.53 (dddd, 1H, *J*=10.0, 4.7, 2.9, 1.8 Hz, H-5), 5.64 (dddd, 1H, *J*=10.0, 4.1, 2.6, 1.7 Hz, H-6), 6.31 (d, 1H, *J*=7.8 Hz, H-12), 6.39 (d, 1H, *J*=7.8 Hz, H-11), 6.44 (dd, 1H, *J*=8.1, 1.9 Hz, H-20), 6.49 (dd, 1H, *J*=8.0, 1.9 Hz, H-19), 6.66 (dd, 1H, *J*=7.7, 1.9 Hz, H-17), 6.69 (dd, 1H, *J*=7.7, 1.9 Hz, H-16); ^{13}C NMR δ 17.3 (Me), 28.9 (C-13), 31.5 (C-4), 32.3 (C-2), 33.5 (C-7), 34.5 (C-1 or C-14), 35.0 (C-3b), 35.2 (C-1 or C-14), 92.4 (C-7a), 122.2 (C-3a), 123.3 (C-6), 127.1 (C-10), 128.9 (C-5), 130.3 (C-19 or C-20), 131.0 (C-19 or C-20), 132.4 (C-12), 132.4 (C-17), 133.0 (C-16), 135.9 (C-11), 138.5 (C-3, C-15, or C-18), 138.51 (C-3, C-15, or C-18), 140.0 (C-3, C-15, or C-18), 148.2 (C-9a), 160.7 (C-8). Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 74.23; H, 5.86; N, 3.58.

5.2.2. Compound 4b. Purified by column chromatography eluting with 9:1 petroleum ether/EtOAc; mp 184–185 °C (hexane/EtOAc); IR: 1765 (s, C═O), 1554 (C–NO_2) cm^{-1}; ^{1}H NMR δ 1.22 (d, 3H, *J*=7.2 Hz, 7-Me), 1.52 (ddd, 1H, *J*=18.4, 8.6, 3.9 Hz, H-4), 1.80 (ddd, 3H, *J*=2.2, 2.1, 1.6 Hz, 6-Me), 2.46 (ddd, 1H, *J*=18.4, 8.2, 3.3 Hz, H-4), 2.79 (ddd, 1H, *J*=13.9, 10.6, 3.7 Hz, H-13), 2.94–3.26 (m, 6H, H-1, H-2, H-14), 3.29 (br d, 1H, *J*=7.2 Hz, H-7), 3.38 (ddd, 1H, *J*=13.9, 10.2, 4.5 Hz, H-13), 4.12 (dd, 1H, *J*=8.6, 8.2 Hz, H-3b), 5.16 (ddd, 1H, *J*=3.9, 3.3, 2.1 Hz, H-5), 6.27 (d, 1H, *J*=7.8 Hz, H-12), 6.34 (d, 1H, *J*=7.8 Hz, H-11), 6.35 (dd, 1H, *J*=8.2, 1.8 Hz, H-20), 6.42 (dd, 1H, *J*=8.2, 1.9 Hz, H-19), 6.68 (dd, 1H, *J*=7.8, 1.9 Hz, H-17), 6.69 (dd, 1H, *J*=7.8, 1.8 Hz, H-16); ^{13}C NMR δ 15.3 (7-Me), 21.9 (6-Me), 28.7 (C-13), 31.5 (C-4), 32.7 (C-7), 32.8 (C-1, C-2, or C-14), 34.7 (C-1, C-2, or C-14), 35.5 (C-1, C-2, or C-14), 38.4 (C-3b), 92.9 (C-7a), 118.2 (C-5), 122.0 (C-3a), 126.9 (C-10), 130.7 (C-19 or C-20), 132.0 (C-19 or C-20), 132.3 (C-12), 132.4 (C-17), 133.1 (C-16), 135.6 (C-6), 136.2 (C-11), 137.9 (C-3, C-15, or C-18), 138.7 (C-3, C-15, or C-18), 140.1 (C-3, C-15, or C-18), 148.0 (C-9a), 160.5 (C-8). Anal. Calcd for $C_{25}H_{25}NO_4$: C, 74.42; H, 6.25; N, 3.47. Found: C, 74.33; H, 6.21; N, 3.56.

5.2.3. Compound 4c. Purified by column chromatography eluting with 9:1 petroleum ether/EtOAc; mp 150–151 °C (hexane); IR: 2401 (s, C–N), 1712 (s, C═O), 1552 (C–NO_2) cm^{-1}; ^{1}H NMR δ 1.49 (ddd, 1H, *J*=19.3, 9.4, 2.9 Hz, H-4), 2.46 (ddd, 1H, *J*=19.3, 7.5, 4.6 Hz, H-4), 2.80 (ddd, 1H, *J*=13.9, 10.6, 4.0 Hz, H-13), 2.94–3.18 (m, 4H, H-1, H-14), 3.22 (m, 1H, H-2), 3.32 (m, 1H, H-2), 3.37 (ddd, 1H, *J*=13.9, 10.1, 4.4 Hz, H-13), 3.48 (s, 3H, OMe), 4.23 (dd, 1H, *J*=9.4, 7.5 Hz, H-3b), 4.78 (br d, 1H, *J*=4.1 Hz, H-7), 5.78 (ddd, 1H, *J*=10.1, 4.6, 2.9 Hz, H-5), 6.04 (dd, 1H, *J*=10.1, 4.1 Hz, H-6), 6.29 (d, 1H, *J*=7.7 Hz, H-12), 6.29 (dd, 1H, *J*=8.1, 1.6 Hz, H-19), 6.37 (d, 1H, *J*=7.7 Hz, H-11), 6.45 (dd, 1H, *J*=8.1, 1.6 Hz, H-20), 6.69 (dd, 1H, *J*=7.8, 1.6 Hz, H-16), 6.73 (dd, 1H, *J*=7.8, 1.6 Hz, H-17); ^{13}C NMR δ 28.7 (C-13), 31.1 (C-4), 32.7 (C-3b), 33.2 (C-2), 34.7 (C-14), 35.6 (C-1), 58.8 (OMe), 73.9 (C-7), 90.5 (C-7a), 120.7 (C-3a), 123.9 (C-6), 126.9 (C-10), 128.9 (C-5), 130.6 (C-19 and C-20), 132.2 (C-12), 132.4 (C-16 or C-17), 133.1 (C-16 or C-17), 136.6 (C-11), 138.1 (C-3, C-15, or C-18), 138.8 (C-3, C-15, or C-18), 140.0 (C-3, C-15, or C-18), 148.0 (C-9a), 159.3 (C-8). Anal. Calcd for $C_{24}H_{23}NO_5$: C, 71.10; H, 5.72; N, 3.45. Found: C, 71.30; H, 5.66; N, 3.39.

5.2.4. Compound 5. Purified by column chromatography eluting with 9:1 petroleum ether/EtOAc; mp 153–154 °C (hexane); IR: 2401 (s, C–N), 1710 (s, C═O), 1522 (C–NO_2) cm^{-1}; ^{1}H NMR δ 2.23 (ddd, 1H, *J*=18.3, 6.8, 4.2 Hz, H-4), 2.45 (ddd, 1H, *J*=18.3, 6.9, 4.1 Hz, H-4), 2.72 (ddd, 1H, *J*=13.8, 10.5, 4.5 Hz, H-13), 2.95–3.11 (m, 5H, H-1, H-2, H-14), 3.20 (m, 1H, H-2), 3.33 (s, 3H, OMe), 3.41 (ddd, 1H, *J*=13.8, 10.3, 3.9 Hz, H-13), 4.02 (dd, 1H, *J*=6.9, 6.8 Hz, H-3b), 4.74 (br d, 1H, *J*=3.3 Hz, H-7), 5.79 (ddd, 1H, *J*=10.0, 4.2, 4.1 Hz, H-5), 5.99 (dd, 1H, *J*=10.0, 3.3 Hz, H-6), 6.35 (d, 1H, *J*=7.8 Hz, H-12), 6.42 (d, 1H, *J*=7.8 Hz, H-11), 6.53–6.63 (m, 3H, H-16, H-19, H-20), 6.67 (m, 1H, H-17); ^{13}C NMR δ 29.5 (C-13), 29.6 (C-4), 33.6 (C-2), 34.4 (C-14), 34.8 (C-1), 37.8 (C-3b), 59.0 (OMe), 77.4 (C-7), 92.5 (C-7a), 121.3 (C-3a), 125.5 (C-6), 127.4 (C-10), 127.5 (C-5), 129.8 (C-19), 130.1 (C-12 or C-20), 132.1 (C-12 or C-20), 132.8 (C-16 or C-17), 133.0 (C-16 or C-17), 135.3 (C-11), 138.2 (C-3, C-15, or C-18), 138.3 (C-3, C-15, or C-18), 140.1 (C-3, C-15, or C-18), 149.1 (C-9a), 159.8 (C-8). Anal. Calcd for $C_{24}H_{23}NO_5$: C, 71.10; H, 5.72; N, 3.45. Found: C, 70.89; H, 5.80; N, 3.48.

5.2.5. Compound 4d. Purified by column chromatography eluting with 9:1 petroleum ether/EtOAc; mp 150–151 °C (hexane); IR: 2338 (s, C–N), 1770 (s, C═O), 1563 (C–NO_2) cm^{-1}; ^{1}H NMR δ 2.31 (dddd, 1H, *J*=17.7, 5.8, 1.9, 1.7 Hz, H-4), 2.47 (dddd, 1H, *J*=17.7, 6.9, 2.0, 1.9 Hz, H-4), 2.75 (ddd, 1H, *J*=13.7, 10.7, 4.3 Hz, H-13), 2.95 (ddd, 1H, *J*=17.0, 2.0, 1.9 Hz, H-7), 3.00–3.28 (m, 6H, H-1, H-2, H-14), 3.08 (ddd, 1H, *J*=17.0, 1.9, 1.7 Hz, H-7), 3.37 (ddd, 1H, *J*=13.7, 10.3, 3.9 Hz, H-13), 3.51 (s, 3H, OMe), 3.55 (s, 3H, OMe), 4.13 (dd, 1H, *J*=6.9, 5.8 Hz, H-3b), 6.39 (d, 1H, *J*=7.7 Hz, H-12), 6.46 (d, 1H, *J*=7.7 Hz, H-11), 6.47 (dd, 1H, *J*=8.0, 1.9 Hz, H-20), 6.59 (dd, 1H, *J*=8.0, 1.9 Hz, H-19), 6.63 (dd, 1H, *J*=7.7, 1.8 Hz, H-16), 6.66 (dd, 1H, *J*=7.7, 1.9 Hz, H-17); ^{13}C NMR δ 29.4 (C-13), 29.7 (C-4 or C-7), 30.5 (C-4 or C-7), 33.9 (C-2), 34.3 (C-1 or C-14), 34.9 (C-1 or C-14), 37.7 (C-3b), 58.1(OMe in C-5 or C-6), 58.2 (OMe in C-5 or C-6), 89.6 (C-7a), 121.8 (C-3a), 127.7 (C-10), 129.5 (C-19), 130.1 (C-20), 132.1 (C-6), 132.8 (C-12), 132.9 (C-16 and C-17), 135.2 (C-2), 135.7 (C-11), 138.3 (C-15), 139.2 (C-3), 139.9 (C-18), 148.7 (C-9a), 160.9 (C-8). Anal. Calcd for $C_{25}H_{25}NO_6$: C, 68.95; H, 5.79; N, 3.22. Found: C, 68.86; H, 5.82; N, 3.26.

5.2.6. Compound 6. Purified by column chromatography eluting with 4:1 petroleum ether/toluene; mp 165–166 °C (hexane/EtOAc); IR: 1733 (s, C═O), 1563 (C–NO_2) cm^{-1}; ^{1}H NMR δ 2.18 (m, 1H, H-6), 2.48 (ddd, 1H, *J*=13.5, 3.3, 3.2 Hz, H-6), 2.63 (m, 1H, H-4), 2.66 (m, 1H, H-7), 2.70 (m, 1H, H-17), 2.76 (m, 1H, H-4), 2.95–3.14 (m, 4H, H-1, H-18), 3.01 (m, 1H, H-7), 3.08 (m, 1H, H-2), 3.28 (m, 1H, H-2), 3.51 (ddd, 1H, *J*=13.2, 10.2, 3.0 Hz, H-4), 4.08 (dddd, 1H, *J*=3.5, 2.8, 2.3, 1.1 Hz, H-11b), 4.31 (dd, 1H,

J=7.6, 3.1 Hz, H-3b), 5.61 (dddd, 1H, J=5.0, 2.9, 2.8, 2.4 Hz, H-5), 6.51 (d, 1H, J=7.9 Hz, H-16), 6.54 (d, 1H, J=7.9 Hz, H-15), 6.62 (m, 1H, H-20), 6.63 (dd, 1H, J=8.1, 1.9 Hz, H-23), 6.64 (m, 1H, H-21), 6.78 (dd, 1H, J=8.1, 2.0 Hz, H-24), 7.11 (m, 1H, H-8), 7.14–7.19 (m, 2H, H-9, H-10), 7.22 (m, 1H, H-11); ^{13}C NMR δ 30.1 (C-4 or C-17), 30.11 (C-7), 33.5 (C-6), 34.0 (C-18), 34.5 (C-1), 35.4 (C-2), 41.0 (C-3b and C-11b), 95.1 (C-11c), 119.8 (C-5), 125.8 (C-3a), 126.4 (C-9 or C-10), 127.3 (C-9 or C-10), 127.9 (C-23), 128.0 (C-14), 128.4 (C-11), 129.1 (C-24), 129.3 (C-8), 132.4 (C-16), 132.6 (C-11a), 133.0 (C-21), 133.2 (C-20), 134.8 (C-15), 135.1 (C-5a), 138.3 (C-22), 139.9 (C-19), 140.9 (C-3), 141.4 (C-7a), 148.6 (C-13a), 162.1 (C-12). Anal. Calcd for $C_{31}H_{27}NO_4$: C, 77.97; H, 5.70; N, 2.93. Found: C, 77.79; H, 5.72; N, 2.97.

5.2.7. Compound 7. Purified by column chromatography eluting with 4:1 petroleum ether/toluene; mp 196–197 °C (hexane/EtOAc); IR: 1777 (s, C=O), 1563 (C–NO_2) cm^{-1}; ^{1}H NMR δ 1.62 (ddd, 1H, J=19.0, 9.0, 3.8 Hz, H-4), 2.31 (m, 1H, H-6), 2.53 (m, 1H, H-6), 2.61 (ddd, 1H, J=19.0, 8.6, 3.8 Hz, H-4), 2.71 (m, 1H, H-7), 2.75 (m, 1H, H-18), 2.82 (m, 1H, H-17), 2.92 (m, 1H, H-1), 3.02 (m, 1H, H-7), 3.05 (m, 2H, H-2, H-18), 3.16 (m, 1H, H-1), 3.24 (m, 1H, H-2), 3.26 (m, 1H, H-17), 4.34 (dd, 1H, J=9.0, 8.6 Hz, H-3b), 4.54 (ddd, 1H, J=3.3, 2.7, 2.5 Hz, H-11b), 5.42 (ddd, 1H, J=3.8, 3.3, 1.6 Hz, H-5), 6.23 (d, 1H, J=7.7 Hz, H-16), 6.31 (d, 1H, J=7.7 Hz, H-15), 6.35 (dd, 1H, J=8.1, 1.8 Hz, H-23), 6.40 (dd, 1H, J=8.1, 1.8 Hz, H-24), 6.68 (dd, 1H, J=7.6, 1.8 Hz, H-21), 6.72 (dd, 1H, J=7.6, 1.8 Hz, H-20), 6.99 (dd, 1H, J=7.4, 1.1 Hz, H-11), 7.16 (m, 1H, H-10), 7.17 (dd, 1H, J=7.1, 1.2 Hz, H-8), 7.21 (m, 1H, H-9); ^{13}C NMR δ 28.4 (C-17), 31.0 (C-1 or C-18), 31.3 (C-7), 33.7 (C-6), 33.9 (C-4), 34.9 (C-1 or C-18), 35.6 (C-2), 40.2 (C-3b), 46.5 (C-11b), 93.8 (C-11c), 119.0 (C-5), 121.0 (C-3a), 126.5 (C-9 or C-10), 126.9 (C-14), 127.2 (C-11), 127.5 (C-9 or C-10), 128.9 (C-8), 131.8 (C-23 or C-24), 132.0 (C-23 or C-24), 132.4 (C-16), 132.5 (C-20 or C-21), 132.69 (C-11a), 132.7 (C-20 or C-21), 135.7 (C-5a), 136.6 (C-15), 136.9 (C-3), 138.6 (C-19 or C-22), 140.1 (C-19 or C-22), 141.7 (C-7a), 148.2 (C-13a), 158.2 (C-12). Anal. Calcd for $C_{31}H_{27}NO_4$: C, 77.97; H, 5.70; N, 2.93. Found: C, 78.05; H, 5.67; N, 2.90.

Acknowledgements

L.M., A.M., S.L., and M.S. are grateful to the M.I.U.R. (Ministero dell'Istruzione, dell'Università e della Ricerca) Rome, Italy for the financial support. E.G.-B. thanks the Hungarian Academy of Sciences. The authors thank Maria Cristina Ginnasi for assistance in the synthesis.

References and notes

1. Minuti, L.; Marrocchi, A.; Tesei, I.; Gacs-Baitz, E. *Tetrahedron Lett.* **2005**, *46*, 8789.
2. (a) Zheng, H.; Zhang, R.; Wu, F.; Tian, W.; Shen, J. *Synth. Met.* **1999**, *100*, 291; (b) Kaur, A.; Cazeca, M. J.; Sengupta, S. K.; Kumar, J.; Tripathy, S. K. *Synth. Met.* **2002**, *126*, 283; (c) Bartholomew, G. P.; Ledoux, I.; Mukamel, S.; Bazan, G. C.; Zyss, J. *J. Am. Chem. Soc.* **2002**, *124*, 13480; (d) Ping, C. J.; Kazomuri, U.; Koichi, S. U.S. Patent 309,116, December 4, 2002; (e) Trenor, S. R.; Shultz, A. R.; Love, B. J.; Long, T. E. *Chem. Rev.* **2004**, *104*, 3059; (f) Hu, W.; Pflaum, J.; Scweitzer, D.; Dressel, M. *Appl. Phys. Lett.* **2004**, *84*, 4720.
3. (a) Minuti, L.; Taticchi, A.; Marrocchi, A.; Landi, S.; Gacs-Baitz, E. *Tetrahedron Lett.* **2005**, *46*, 5735; (b) Taticchi, A.; Minuti, L.; Marrocchi, A.; Lanari, D. *Recent Res. Dev. Org. Chem.* **2004**, 477; (c) Taticchi, A.; Minuti, L.; Lanari, D.; Marrocchi, A.; Tesei, I.; Gacs-Baitz, E. *Tetrahedron* **2004**, *60*, 11759; (d) Minuti, L.; Taticchi, A.; Lanari, D.; Marrocchi, A.; Gacs-Baitz, E. *Tetrahedron: Asymmetry* **2003**, *14*, 2775; (e) Minuti, L.; Taticchi, A.; Lanari, D.; Marrocchi, A.; Gacs-Baitz, E. *Tetrahedron: Asymmetry* **2003**, *14*, 2387; (f) Minuti, L.; Taticchi, A.; Marrocchi, A.; Costantini, L.; Gacs-Baitz, E. *Tetrahedron: Asymmetry* **2001**, *12*, 1179.
4. (a) Ohkata, K.; Miyamoto, K.; Matsumura, S.; Akiba, K. *Tetrahedron Lett.* **1993**, *34*, 6575; (b) Minami, T.; Matsumoto, Y.; Nakamura, S.; Koyanagi, S.; Yamaguchi, M. *J. Org. Chem.* **1992**, *57*, 167; (c) Ohkata, K.; Lee, Y.-G.; Utsumi, Y.; Ishmaru, K.; Akiba, K. *J. Org. Chem.* **1991**, *56*, 5052; (d) Amantini, D.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2003**, *68*, 9263; (e) Girotti, R.; Marrocchi, A.; Minuti, L.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2006**, *71*, 70.
5. (a) Hopf, H. *Classics in Hydrocarbon Chemistry*; Wiley-VCH GmbH: Weinheim, 2000; pp 321–378; (b) Vögtle, F. *Cyclophane Chemistry*; Wiley-Sons: New York, NY, 1993; (c) Reiss, J. A. *Cyclophanes*; Keehn, P. M., Rosenfeld, S. M., Eds.; Academic: New York, NY, 1983.
6. (a) Matsumoto, K.; Achenson, R. M. *Organic Synthesis at High Pressure*; J. Wiley and Sons: New York, NY, 1991; (b) Minuti, L.; Taticchi, A.; Costantini, L. *Recent Res. Dev. Org. Chem.* **1999**, *3*, 105 and references cited therein.
7. (a) Minuti, L.; Taticchi, A.; Marrocchi, A.; Gacs-Baitz, E.; Galeazzi, R. *Eur. J. Org. Chem.* **1999**, *11*, 3155; (b) Marrocchi, A.; Minuti, L.; Taticchi, A.; Dix, I.; Hopf, H.; Gacs-Baitz, E.; Jones, P. G. *Eur. J. Org. Chem.* **2001**, 4259; (c) Marrocchi, A.; Minuti, L.; Taticchi, A.; Scheeren, H. W. *Tetrahedron* **2001**, *57*, 4959.
8. (a) Fringuelli, F.; Taticchi, A. *Diels–Alder reaction*; J. Wiley and Sons: New York, NY, 1990; (b) Fringuelli, F.; Taticchi, A. *Diels–Alder reaction: Selected Practical Methods*; J. Wiley and Sons: New York, NY, 2002.
9. Minuti, L.; Taticchi, A.; Gacs-Baitz, E.; Marrocchi, A. *Tetrahedron* **1995**, *51*, 8953.