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Double Methylenecyclopentane Annulation of Succinimides: Easy Access to 3,7-Dioxobicyclo[3.3.0]octane-1,5-dicarboximides

Pelayo Camps,*[a] José A. Fernández,[a] Jordi Rull,[a] and Santiago Vázquez[a]

Dedicated to Prof. Dr. Armin de Meijere on the occasion of his 70th birthday

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N-Alkylsuccinimides reacted with excess of LHMDS and 3-chloro-2-(chloromethyl)-1-propene to give in medium yields *N*-alkyl-3,7-dimethylenebicyclo[3.3.0]octane-1,5-dicarboximides, which were ozonized to the corresponding 3,7-dioxobicyclo[3.3.0]octane-1,5-dicarboximides. When these alkylations were carried out by using LDA as the base, *cis*-*N*-alkyl-4-methylenecyclopentane-1,2-dicarboximides were mainly obtained, in spite of using excess of both base and alkylating agent.

Introduction

Many *cis*-bicyclo[3.3.0]octane-3,7-diones mono- or disubstituted at the bridgehead positions **1** (Figure 1) are readily available compounds through the Bertz–Weiss–Cook reaction.[1] These compounds have been used for the synthesis of many polyquinenes, such as staurane-2,5,8,11-tetraene, modhephene, triquinacene, polyquinane natural products, such as gymnomitrol, quadrone, isocomene, pentalenene, and non-natural products, such as semibullvalenes, [5]peristylane, among others.[2]

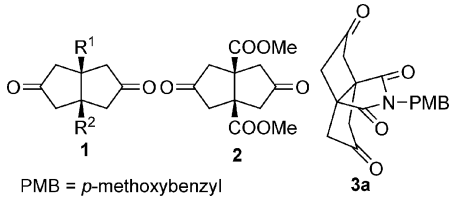
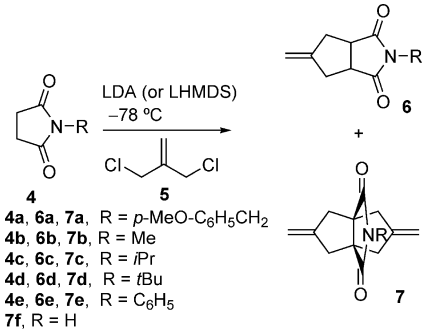


Figure 1. Diketones from the Bertz–Weiss–Cook reaction and derivative thereof.

To the best of our knowledge, the only described *cis*-bicyclo[3.3.0]octane-3,7-dione having two carbonyl substituents at the bridgehead positions directly obtained via the Bertz–Weiss–Cook reaction is dimethyl *cis*-3,7-dioxobicyclo[3.3.0]-octane-1,5-dicarboxylate (**2**), which was prepared several years ago by our research group.[3] Disodium dihydroxytartrate was esterified with MeOH/HCl, the crude dimethyl 2,3-dioxobutanedioate or derivative thereof thus obtained was condensed with dimethyl acetonedicarboxylate and the mixture of condensation products was directly submitted to methoxydecarboxylation under the Krapcho conditions[4] to give **2** in only 18% yield. Deslongchamps et al.[5] found that this is an unusual Bertz–Weiss–Cook condensation in which an oxabicyclic intermediate instead of the expected carbobicyclic diketo ester is formed. Demethoxycarboxylation of this oxabicyclic intermediate under the Krapcho conditions gives **2**, probably via the usual carbobicyclic diketo ester.

This research group transformed compound **2** in three steps into compound **3a**, as a key intermediate for the preparation of a novel scaffold for the modular assembly of re-



Scheme 1. Mono- and bis-annulations of succinimides **4**.

[a] Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, and Institute of Biomedicine (IBUB), Universitat de Barcelona,
Av. Diagonal 643, 08028 Barcelona, Spain
Fax: +34-93-4035941
E-mail: camps@ub.edu

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ceptor models (Figure 1).[6] However, the preparation of **3a** is lengthy and low-yielding. Other transformations from **2** were also carried out by the same group.[7]

Our continued interest on diones **1** as starting compounds to prepare functionalized tricyclo[3.3.0.0^{3,7}]octane derivatives,[8] led us to plan an alternative and shorter procedure to prepare compound **3a** and related compounds from readily available starting materials, as shown in Scheme 1.

Results and Discussion

It is known that diethyl *trans*-4-methylenecyclopentane-1,2-dicarboxylate can be obtained from succinic acid by (i) conversion into a bis-oxazoline derivative by reaction with 2-amino-2,2-dimethylethanol, (ii) alkylation of the corresponding dianion, generated by reaction with *n*BuLi, with 3-chloro-2-(chloromethyl)-1-propene (**5**) and (iii) ethanolysis.[9] Also, diastereo-enriched di-(–)-menthyl *trans*-4-methylenecyclopentane-1,2-dicarboxylate has been obtained by reaction of the dianion of di-(–)-menthyl succinate with the above dialkylating agent **5** using 2,2,6,6-tetramethylpiperidide as the base.[10] Moreover, we had experience in the formation of cyclopentane derivatives by alkylation of a dianion derived from an *N*-aryl-α,α′-disubstituted succinimide with 1,3-dibromopropane using LDA as the base,[11] following a known procedure.[12]

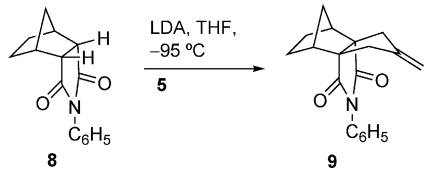
Consequently, we imagined that reaction of *N*-substituted succinimides **4** with an excess of a base, such as LDA, and an excess of the alkylating agent **5** might give imides **6** which could be further alkylated to give finally imides **7** (Scheme 1).

Succinimide **4a** was prepared by a known procedure,[13] succinimide **4b** is commercially available, succinimide **4c**[14] was prepared in good yield by the same procedure described for **4a**,[13] and succinimide **4d**[14] was obtained by a known procedure.[15] Results of the alkylation of different succinimides **4** with **5** are collected in Table 1. Worthy of note, using lithium diisopropylamide (LDA) as the base, monoannulated products **6** were usually isolated in medium (49–65%) yields as the only defined reaction products, in spite of using a great excess of base and alkylating agent (Entries 1, 7, 9 and 11). The rest of material could not be identified. Only in one case (Entry 5) starting from **4b** and using lower excesses of base (4.5 equiv.) and alkylating agent (2.4 equiv.), monoannulated and diannulated products **6b** (34%) and **7b** (23%), respectively, were isolated. Contrarily, using lithium hexamethyldisilazide (LHMDS) as the base, under similar reaction conditions, diannulated products **7** were obtained in 36–79% yield (Entries 2, 4, 8, 10 and 12), monannulated products **6** being not detected. The best yield was obtained for the *N*-(*p*-methoxybenzyl) derivative **7a** (79%, Entry 2) and then for the *tert*-butyl derivative **7d** (69%, Entry 12). However, the yield of the *N*-methyl derivative **7b** was low (36%, Entry 8). Reaction of compound **6a** with LDA (3 equiv.) and **5** (2 equiv.) under the usual conditions gave **7a** in 54% yield (Entry 4), thus showing that LDA is an adequate base to prepare double-annulated products (**7**) from monoannulated ones (**6**). Reaction of succinimide **4a** with **5** using lithium 2,2,6,6-tetramethylpiperidide (LTMP) as the base under standard conditions (great excess of base and **5**) gave mainly monoannulated product **6a** and traces of diannulated product **7a** (Entry 3). As before, reaction of **6a** with **5** using LTMP as the base gave **7a** although in only 24% yield. These results might be partly understood on the basis of steric effects, the less bulky base (LDA) acting as a nucleophile might participate in side reactions whether with the alkylating agent or the succinimide in a greater extent, while the more bulky base (LTMP) might be not so adequate for the alkylation of the monoannulated products **6**.

Table 1. Conditions, products and yields from the reaction of succinimides **4** and **6a** with **5**.

Entry	Compd.	**5** (equiv.)	Base (equiv.)	Product **6** (%)	**7** (%)
1	**4a**	4.0	LDA (6.0)	65	–
2	**4a**	4.0	LHMDS (6.0)	–	79
3	**4a**	4.0	LTMP (6.0)	24	3
4	**6a**	2.0	LDA (3.0)	–	54
5	**6a**	2.0	LTMP (3.0)	–	24
6	**4b**	2.4	LDA (4.5)	34	23
7	**4b**	4.3	LDA (6.0)	49	–
8	**4b**	4.3	LHMDS (6.0)	–	36
9	**4c**	3.9	LDA (6.0)	53	–
10	**4c**	4.0	LHMDS (6.1)	–	47
11	**4d**	4.0	LDA (6.0)	50	–
12	**4d**	4.0	LHMDS (6.0)	–	69
13	**4e**	2.4	LDA (5.0)	–	–
14	**4e**	2.4	LHMDS (5.0)	–	–

Curiously, no mono- or bis-annelated products were ever isolated starting from *N*-phenylsuccinimide **4e** using either LDA or LHMDS as the base. This result is in striking contrast with a parallel transformation performed by the group starting from the *N*-phenylsuccinimide derivative **8**, which gave the annulated product **9** in 65% yield (Scheme 2).



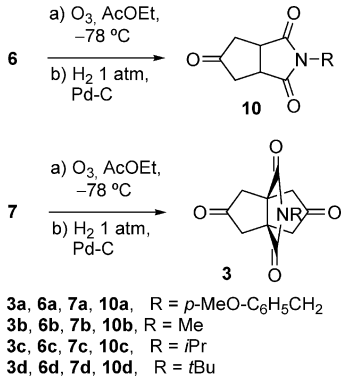
8 9

Scheme 2. Successful annulation of the *N*-phenylimide **8**.

The *p*-methoxybenzyl group of imide **7a** could be cleaved by treatment with Cerium(IV) ammonium nitrate (CAN) in the usual way[16] to give the corresponding deprotected imide **7f** in 67% yield.

The new mono- and bis-annulated products **6a–d/7a–d** were submitted to ozonization leading, after hydrogenation of the ozonide, to the corresponding mono- or di-ketones

(**10** or **3**) in high yields (Scheme 3).[17] Other oxidation methods based on ruthenium or osmiun tetraoxide and $NaIO_4/KMnO_4$ failed to give the desired ketones.[18–20] Except dioxoimide **3a**[6] and oxoimide **10b**,[21] the rest of compounds **3**, **6**, **7**, **9** and **10** described herein are novel and have been fully characterized through their spectroscopic data as well as elemental analysis and/or HRMS. Several of the prepared compounds, especially those containing more carbonyl functions, retain molecules of water in spite of being carefully dried under high vacuum. It is known that inclusion of water in organic crystals is very common due to the small size of the water molecule and its excellent hydrogen bonding ability. As stated by G. R. Desiraju,[22] "the proportion of non-ionic, metal-free, organic compounds that crystallize as hydrates increases, within the class, with an increase in the number of hydrogen-bond acceptor groups with respect to the donor groups".



Scheme 3. Oxidation of alkenes **6**/**7** to the corresponding ketones **10**/**3**.

According to a referee, the presence of water in one of these compounds (**6a**) was established by ^1H NMR, as follows: (a) First, we obtained the spectrum of the solvent ($CDCl_3$) containing tetramethylsilane (TMS) as internal reference, collecting 32 scans with a delay of 25 s to facilitate relaxation of all kind of protons, (b) solid compound **6a** was then added to the NMR tube and once dissolved the sample, a new spectrum was collected under the same conditions (See Supporting Information). The ratio of the integral of the TMS and the signal of water at δ = 1.53 ppm was 100:79.4 in the spectrum of the solvent alone and 100:91.6 in the spectrum of the solvent plus **6a**. Taking into account the values for the integral of two protons of **6a** in all the signals except the one overlapping with $CHCl_3$ (minimum value: 90.1; maximum value: 92.7; average value: 91.6), a molar ratio water/**6a** = 0.13 was calculated, in good concordance with the elemental analysis which agrees with a molar ratio water/**6a** = 0.15. A similar experiment carried out with compound **10c** showed also the presence of water, although calculations could not be so clearly performed due to overlapping of the signals of water and the methyl groups from the isopropyl substituent. For similar reasons, this kind of experiment was not performed for the rest of compounds (**3d**, **6c** and **7c**) whose elemental analyses also suggest the presence of water.

A compound **6** (R = H), has been used as an intermediate in the preparation of SC-52491 and SC-52490, two azanoradamantane benzamide derivatives which exhibit very potent affinity for both the serotonin 5-HT_4 and 5-HT_3 receptors.[23,24] We are currently pursuing the application of ketones **3** and **10** or diene **7** for the preparation of new functionalized cage compounds related to those previously prepared by the group,[8] as scaffolds for potentially active compounds.[25,26]

Conclusions

We have developed a two-step synthesis of diketoimides **3**, that can be readily performed on gram scale now. The key-step consists of a double methylenecyclopentane annulation of *N*-substituted succimides by alkylation with 3-chloro-2-(chloromethyl)-1-propene (**5**). The preparation of the known **3a** in 64% yield greatly improves the previous preparation from diketone **2**, obtained through the Bertz–Weiss–Cook reaction. Similarly, ketoimides **10** have been obtained which, together with the corresponding alkene precursors **7** and **6**, constitute a series of interesting synthetic intermediates.

Experimental Section

General Methods: Melting points were determined in open capillary tubes. Unless otherwise stated, NMR spectra were recorded at 25 °C in $CDCl_3$: ^1H NMR (400 MHz), ^{13}C NMR (100.6 MHz). Chemical shifts (δ) are reported in ppm related to internal standard ($CHCl_3$ at δ_H = 7.26 ppm, δ_C = 77.0 ppm). Assignments given for the NMR spectra are based on DEPT sequence, $^1H/^1H$ COSY, $^1H/^{13}C$ HETCOR (HSQC sequence) and $^1H/^1H$ NOESY experiments for selected compounds. Unless otherwise stated, IR spectra were performed with the attenuated total reflection (ATR) technique and the absorption values are given as wavenumbers (cm^{-1}). Elemental analyses were done at the Microanalysis Service of the IIQAB (CSIC, Barcelona, Spain). Column chromatography was performed on silica gel 60 A C.C. (35–70 mesh). For the thin-layer chromatography (TLC), aluminum-backed sheets with silica gel 60 F_{254} were used and spots were visualized with UV light and/or 1% aqueous $KMnO_4$.

***N*-(*p*-Methoxybenzyl)-4-methylene-*cis*-cyclopentane-1,2-dicarboximide (6a):** A solution of *n*BuLi in hexanes (44.0 mL, 2.50 M, 110 mmol) was added to a cold (0 °C) solution of anhydrous diisopropylamine (15.4 mL, 110 mmol) in anhydrous THF (100 mL), and the mixture was allowed to react for 1 h at this temperature. Then, a solution of succinimide **4a** (4.00 g, 18.2 mmol) in anhydrous THF (65 mL) was added, the solution was stirred for 15 min at –78 °C and then it was warmed to 0 °C in 1 h. The solution was cooled to –78 °C and dichloride **5** (8.50 mL, 73.4 mmol) in anhydrous THF (40 mL) was added dropwise. The mixture was warmed to room temperature and stirred for 3 d at this temperature. The mixture was made acidic with aqueous 2 N HCl (125 mL) and extracted with Et_2O (3 × 150 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo, and the residue (7.66 g) was subjected to column chromatography [silica gel (154 g), hexane/AcOEt, 1:1] to yield alkene **6a** (3.22 g, 65% yield) as a pale yellow solid. The analytical sample was obtained as a white solid by crystallization from AcOEt/hexane, 8:5, m.p. 106–107 °C; R_f =

0.54 (hexane/AcOEt, 2:1). IR (KBr): $\tilde{\nu}$ = 3019, 2971, 2959, 2936, 2906, 2839, 1766, 1707, 1694, 1611, 1514, 1461, 1431, 1400, 1365, 1350, 1244, 1178, 1028, 926, 914, 816 cm^{-1}. ^{1}H NMR: δ = 2.60 [br. d, J = 16.4 Hz, 2 H, 3(5)-H$_{cis}$], 2.65–2.74 [ddm, J = 16.4, J' = 9.6 Hz, 2 H, 3(5)-H$_{trans}$], 3.21 [m, 2 H, 1(2)-H], 3.77 (s, 3 H, OCH$_3$), 4.56 (s, 2 H, N-CH$_2$), 4.87 (br. s, 2 H, C4=CH$_2$), 6.81 [dm, J = 9.2 Hz, 2 H, Ar-3(5)-H], 7.25 [overlapped dm, 2 H, Ar-2(6)-H] ppm. ^{13}C NMR: δ = 36.1 [CH$_2$, C-3(5)], 41.9 (CH$_2$, N-CH$_2$), 44.3 [CH, C-1(2)], 55.2 (CH$_3$, OCH$_3$), 109.6 (CH$_2$, C-4=*C*H$_2$), 113.9 [CH, Ar-C-3(5)], 128.0 (C, Ar-C-1), 129.8 [CH, Ar-C-2(6)], 145.7 (C, C-4), 159.2 (C, Ar-C-4), 179.5 (C, CON) ppm. HRMS (ES$^+$): calcd. for [M + Na]$^+$ 294.1101; found 294.1099. $C_{16}H_{17}NO_3$·0.15H_2O (274.02): calcd. C 70.13, H 6.36, N 5.11; found C 69.81, H 6.27, N 4.82.

***N*-Methyl-4-methylene-*cis*-cyclopentane-1,2-dicarboximide (6b):** This compound was prepared in a similar manner to that described before for **6a**. From **4b** (1.00 g, 8.84 mmol), **6b** (710 mg, 49%) was obtained. The analytical sample was prepared as a white solid by crystallization from hexane, m.p. 84–86 °C, R_f 0.52 (hexane/AcOEt, 1:1). IR: $\tilde{\nu}$ = 2952, 2909, 2842, 1766, 1686, 1429, 1380, 1312, 1281, 1186, 1156, 1090, 1054, 1000, 964, 916, 872, 763, 676, 622 cm^{-1}. ^{1}H NMR (300 MHz): δ = 2.62 [br. d, J = 16.2 Hz, 2 H, 3(5)-H$_{cis}$], 2.66–2.78 [m, 2 H, 3(5)-H$_{trans}$], 2.96 (s, 3 H, N-CH$_3$), 3.21–3.28 [m, 2 H, 1(2)-H], 4.91 (br. s, 2 H, C4=CH$_2$) ppm. ^{13}C NMR (75.4 MHz): δ = 25.0 (CH$_3$, N-CH$_3$), 36.0 [CH$_2$, C-3(5)], 44.3 [CH, C-1(2)], 109.6 (CH$_2$, C-4=CH$_2$), 145.6 (C, C-4), 179.8 (C, CON) ppm. HRMS (ES$^+$): calcd. for [M + H]$^+$ 166.0863; found 166.0861. $C_9H_{11}NO_2$ (165.19): calcd. C 65.44, H 6.71, N 8.48; found C 65.26, H 6.67, N 8.28.

***N*-Isopropyl-4-methylene-*cis*-cyclopentane-1,2-dicarboximide (6c):** This compound was prepared in a similar manner to that described before for **6a**. From **4c** (500 mg, 3.54 mmol), **6c** (310 mg, 45% yield) was isolated as a pale yellow oil. An analytical sample of **6c** was obtained as colorless oil by microdistillation at 200 °C/2 Torr in a rotary microdistillation equipment. R_f 0.64 (hexane/AcOEt, 3:1). IR: $\tilde{\nu}$ = 2973, 2935, 1768, 1686, 1431, 1395, 1382, 1364, 1309, 1284, 1225, 1176, 1134, 1098, 1052, 1033, 1014, 897, 884, 853, 664 cm^{-1}. ^{1}H NMR: δ = 1.32 [d, J = 7.2 Hz, 6 H, N-CH(C*H*$_3$)$_2$], 2.58 [br. d, J = 16.0 Hz, 2 H, 3(5)-H$_{cis}$], 2.67 [ddm, J = 16.0, J' = 7.6 Hz, 2 H, 3(5)-H$_{trans}$], 3.12 [m, 2 H, 1(2)-H], 4.30 [hept, J = 7.2 Hz, 1 H, N-C*H*(CH$_3$)$_2$], 4.88 (br. s, 2 H, C4=CH$_2$) ppm. ^{13}C NMR δ = 19.2 [CH$_3$, N-CH(*C*H$_3$)$_2$], 36.2 [CH$_2$, C-3(5)], 43.79 [CH, C-1(2)], 43.84 [CH, N-*C*H(CH$_3$)$_2$], 109.3 (CH$_2$, C-4=*C*H$_2$), 145.6 (C, C-4), 179.8 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 194.1176; found 194.1167. $C_{11}H_{15}NO_2$·0.1H_2O (195.05): calcd. C 67.74, H 7.85, N 7.18; found C 67.46, H 7.68, N 6.85.

***N*-*tert*-Butyl-4-methylene-*cis*-cyclopentane-1,2-dicarboximide (6d):** This compound was prepared in a similar manner to that described before for **6a**. From **4d** (3.00 g, 19.3 mmol), **6d** (2.00 mg, 50% yield) was obtained. The analytical sample of **6d** was prepared as a white solid by crystallization from AcOEt/hexane, 1:1, m.p. 104–105 °C, R_f 0.75 (hexane/AcOEt, 5:1). IR: $\tilde{\nu}$ = 2977, 2962, 2925, 1780, 1693, 1433, 1365, 1338, 1306, 1296, 1262, 1206, 1181, 1117, 1061, 1011, 912, 881, 733, 653 cm^{-1}. ^{1}H NMR: δ = 1.54 [s, 9 H, N-C(C*H*$_3$)$_3$], 2.59 [br. d, J = 16.0 Hz, 2 H, 3(5)-H$_{cis}$], 2.69 [ddm, J = 16.0, J' = 7.6 Hz, 2 H, 3(5)-H$_{trans}$], 3.06 [m, 2 H, 1(2)-H], 4.90 (br. s, 2 H, C-4=CH$_2$) ppm. ^{13}C NMR: δ = 28.3 [CH$_3$, N-C(*C*H$_3$)$_3$], 36.6 [CH$_2$, C-3(5)], 44.0 [CH, C-1(2)], 58.3 [C, N-*C*(CH$_3$)$_3$], 109.1 (CH$_2$, C-4=*C*H$_2$), 145.9 (C, C-4), 180.9 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 208.1332; found 208.1326. $C_{12}H_{17}NO_2$ (207.27): calcd. C 69.54, H 8.27, N 6.76; found C 69.47, H 8.37, N 6.65.

***N*-(*p*-Methoxybenzyl)-3,7-dimethylene-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (7a) from 4a:** A solution of *n*BuLi in hexanes (44.0 mL, 2.50 M, 110 mmol) was added to a cold (–78 °C) solution of HMDS (23.0 mL, 110 mmol) in anhydrous THF (100 mL), and the mixture was allowed to react for 1 h at this temperature. Then, a solution of succinimide **4a** (4.00 g, 18.2 mmol) in anhydrous THF (50 mL) was added, the solution was stirred for 15 min at –78 °C and then it was warmed to 0 °C in 1 h. The solution was cooled to –78 °C and dichloride **5** (8.40 mL, 72.6 mmol) in anhydrous THF (100 mL) was added dropwise. The mixture was warmed to room temperature and stirred for 4 d at this temperature. The mixture was made acidic with aqueous 1 N HCl (150 mL) and extracted with Et_2O (3 × 250 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo and the residue (8.00 g) was subjected to column chromatography [silica gel (160 g), hexane/AcOEt, 1:1] yielding diene **7a** (4.64 g, 79% yield) as a yellow solid. The analytical sample was obtained as a white solid by crystallization from hexane, m.p. 102–103 °C; R_f = 0.29 (hexane/AcOEt, 2:1). IR (KBr): $\tilde{\nu}$ = 2956, 2899, 2834, 1769, 1690, 1611, 1509, 1432, 1390, 1341, 1305, 1291, 1244, 1175, 1153, 1032, 984, 906, 810, 729, 651, 640, 614 cm^{-1}. ^{1}H NMR: δ = 2.43 (d, J = 16.0 Hz, 4 H) and 2.75 (d, J = 16.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 3.77 (s, 3 H, OCH$_3$), 4.54 (s, 2 H, N-CH$_2$), 4.82 [br. s, 4 H, C-3(7) = CH$_2$], 6.79 [d, J = 9.0 Hz, 2 H, Ar-3(5)-H], 7.18 [d, J = 9.0 Hz, 2 H, Ar-2(6)-H] ppm. ^{13}C NMR: δ = 41.9 (CH$_2$, N-CH$_2$), 42.6 [CH$_2$, C-2(4,6,8)], 55.2 (CH$_3$, OCH$_3$), 60.4 [C, C-1(5)], 109.5 [CH$_2$, C-3(7) = *C*H$_2$], 113.8 [CH, Ar-C-3(5)], 128.0 (C, Ar-C-1), 129.2 [CH, Ar-C-2(6)], 147.4 [C, C-3(7)], 159.0 (C, Ar-C-4), 180.8 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 324.1594; found 324.1595. $C_{20}H_{21}NO_3$ (323.39): calcd. C 74.28, H 6.55, N 4.33; found C 74.10, H 6.65, N 4.28.

7a from 6a: This compound was prepared in a similar manner to that described before for **6a**. From **6a** (250 mg, 0.92 mmol), LDA [from *n*BuLi in hexanes (1.10 mL, 2.50 M, 2.75 mmol) and diisopropylamine (390 μL, 2.75 mmol)] and **5** (210 μL, 1.84 mmol), **7a** (160 mg, 54% yield) was isolated as a pale yellow solid after column chromatography.

***N*-Methyl-3,7-dimethylene-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (7b):** This compound was prepared in a similar manner to that described for **7a**. From **4b** (1.00 g, 8.84 mmol), **7b** (700 mg, 36% yield) was obtained. The analytical sample was prepared as a white solid by crystallization from AcOEt/hexane, m.p. 90–92 °C, R_f = 0.39 (hexane/AcOEt, 1:1). IR: $\tilde{\nu}$ = 2987, 2949, 2914, 2847, 1769, 1697, 1439, 1426, 1376, 1322, 1275, 1127, 1091, 1023, 998, 907, 887, 730, 662, 654 cm^{-1}. ^{1}H NMR: δ = 2.45 (d, J = 16.0 Hz, 4 H) and 2.78 (d, J = 16.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 2.95 (s, 3 H, N-CH$_3$), 4.86 [br. s, 4 H, C-3(7) = CH$_2$] ppm. ^{13}C NMR (75.4 MHz): δ = 25.2 (CH$_3$, N-CH$_3$), 42.7 [CH$_2$, C-2(4,6,8)], 60.6 [C, C-1(5)], 109.6 [CH$_2$, C-3(7) = *C*H$_2$], 147.4 [C, C-3(7)], 181.2 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 218.1176; found 218.1168. $C_{13}H_{15}NO_2$ (217.27): calcd. C 71.87, H 6.96, N 6.45; found C 71.67, H 7.03, N 6.20.

***N*-Isopropyl-3,7-dimethylene-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (7c):** This compound was prepared in a similar manner to that described for **7a**. From **4c** (2.00 g, 14.2 mmol), **7c** (1.65 g, 47% yield) was obtained. The analytical sample was prepared as a white solid by crystallization from hexane, m.p. 49.8–50.4 °C, R_f = 0.61 (hexane/AcOEt, 1:1). IR (ATR): $\tilde{\nu}$ = 2968, 2914, 1759, 1693, 1435, 1390, 1382, 1363, 1315, 1297, 1269, 1213, 1121, 1093, 1049, 904, 891, 730, 655 cm^{-1}. ^{1}H NMR: δ = 1.32 [d, J = 6.8 Hz, 6 H, N-CH(C*H*$_3$)$_2$], 2.42 (d, J = 16.0 Hz, 4 H) and 2.76 (d, J = 16.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 4.29 [hept, J = 6.8 Hz, 1 H,

N-C*H*(CH_3)$_2$], 4.84 [s, 4 H, C3(7)=*C*H$_2$] ppm. ^{13}C NMR: δ = 19.3 [CH_3, *N*-CH(*C*H$_3$)$_2$], 42.8 [CH_2, C-2(4,6,8)], 44.0 [CH, *N*-*C*H-(CH_3)$_2$], 59.8 [C, C-1(5)], 109.3 [CH_2, C-3(7) = CH_2], 147.6 [C, C-3(7)], 181.3 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 246.1489; found 246.1484. $C_{15}H_{19}NO_2$·0.2H_2O (248.92): calcd. C 72.38, H 7.86, N 5.63; found C 72.14, H 7.73, N 5.41.

***N*-*tert*-Butyl-3,7-dimethylene-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (7d):** This compound was prepared in a similar manner to that described for **7a**. From **4d** (5.00 g, 32.2 mmol), **7d** (5.73 g, 69% yield) was obtained. The analytical sample of **7d** was prepared as a white solid by crystallization from AcOEt/pentane, 5:3, m.p. 92–93 °C, R_f 0.41 (hexane/AcOEt, 1:1). IR (KBr): $\tilde{\nu}$ = 3081, 3014, 2976, 2962, 2915, 2846, 1766, 1698, 1686, 1481, 1465, 1438, 1398, 1369, 1337, 1312, 1295, 1269, 1262, 1239, 1201, 1144, 1023, 896, 887, 732, 646 cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.51 [s, 9 H, *N*-C(CH_3)$_3$], 2.41 (dm, *J* = 16.0 Hz, 4 H) and 2.74 (dm, *J* = 16.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 4.83 [pseudo quint, *J* = 1.7 Hz, 4 H, C3(7)=CH_2] ppm. ^{13}C NMR (75.4 MHz): δ = 28.4 [CH_3, *N*-C(*C*H$_3$)$_3$], 43.2 [CH_2, C-2(4,6,8)], 58.4 [C, *N*-*C*(CH$_3$)$_3$], 59.6 [C, C-1(5)], 108.9 [CH_2, C-3(7) = CH_2], 147.6 [C, C-3(7)], 182.1 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 264.1230; found 264.1222. $C_{16}H_{21}NO_2$ (259.35): calcd. C 74.10, H 8.16, N 5.40; found C 73.69, H 8.27, N 5.20.

3,7-Dimethylene-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (7f): A solution of cerium(IV) ammonium nitrate (CAN, 3.50 g, 6.38 mmol) in water (8 mL) was added dropwise to a solution of **7a** (500 mg, 1.55 mmol) in ACN (8 mL), and the mixture was stirred for 2.5 h at room temperature till no more starting compound (TLC) was observed. The mixture was diluted with water (30 mL) and extracted with AcOEt (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue (557 mg) was taken in abs EtOH (25 mL), aqueous NH_3 (20%, 13 mL) was added, and the mixture was heated in a closed reactor at 100 °C for 2 h. The mixture was cooled to room temperature, the volatile materials were eliminated in vacuo and the solid residue was extracted with hot AcOEt (2 × 30 mL). The combined organic extracts were concentrated in vacuo and the residue (389 mg) was subjected to column chromatography [silica gel (39 g), hexane/AcOEt mixtures]. On elution with hexane/AcOEt, 9:1, **7f** (210 mg, 67% yield) was obtained as a pale yellow solid. The analytical sample was obtained as a white solid by crystallization from hexane/AcOEt, 3:1, m.p. 149–150 °C. IR (KBr): $\tilde{\nu}$ = 3188, 3072, 2991, 2964, 1771, 1704, 1432, 1384, 1350, 1319, 1185, 1138, 1099, 899, 838 cm^{-1}. ^{1}H NMR (300 MHz): δ = 2.44 (br. d, *J* = 16.0 Hz, 4 H) and 2.83 (br. d, *J* = 16.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 4.90 [m, 4 H, C-3(7) = CH_2], 8.60 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz): δ = 42.6 [CH_2, C-2(4,6,8)], 61.8 [C, C-1(5)], 109.7 [CH_2, C-3(7) = *C*H$_2$], 147.2 [C, C-3(7)], 181.6 (C, CON) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 204.1019; found 204.0946. $C_{12}H_{13}NO_2$ (203.24): calcd. C 70.92, H 6.45, N 6.89; found C 71.05, H 6.70, N 6.99.

4-Methylene-*N*-phenyltricyclo[5.2.1.0^{2,6}]decane-2β,6β-dicarboximide (9): A solution of *n*BuLi in hexanes (9.6 mL, 2.5 M, 24.0 mmol) was added to a cold (0 °C) solution of anhydrous diisopropylamine (3.4 mL, 24.0 mmol) in anhydrous THF (30 mL), and the mixture was reacted for 10 min at this temperature. Then, the mixture was cooled to –95 °C and a solution of *N*-phenylbicyclo[2.2.1]heptane-2β,3β-dicarboximide **8** (2.41 g, 10.0 mmol) in anhydrous THF (65 mL) was added, the solution was stirred for 15 min at –95 °C and then it was warmed to 0 °C in 1 h. The solution was cooled to –95 °C and dichloride **5** (1.5 mL, 12.0 mmol) in anhydrous THF (60 mL) was added dropwise. The mixture was warmed to room temperature and stirred for 60 h at this temperature. The mixture was made acidic with 1 N HCl (50 mL), diluted with water (50 mL) and extracted with Et_2O (3 × 75 mL). The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo and the residue (3.40 g) was submitted to column chromatography [silica gel (100 g), hexane/AcOEt, 95:5] yielding **9** (1.90 g, 65% yield) as a white solid. The analytical sample was obtained by crystallization from Et_2O, m.p. 107–108 °C. IR (KBr): $\tilde{\nu}$ = 3078, 2977, 2944, 2883, 1771, 1708, 1591, 1499, 1487, 1433, 1376, 1301, 1284, 1171, 1146, 915, 891, 736, 691, 617 cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.44 [m, 2 H, 8(9)-H$_\beta$], 1.56 (dt, *J* = 10.8, *J*′ = 1.5 Hz, 1 H, 10-H$_{anti}$), 1.69 [m, 2 H, 8(9)-H$_\alpha$], 1.96 (dm, *J* = 10.8 Hz, 1 H, 10-H$_{syn}$), 2.46 [dt, *J* = 16.8, *J*′ = 2.4 Hz, 2 H, 3(5)-H$_\beta$], 2.63 [m, 2 H 1(7)-H], 2.93 [dm, *J* = 16.8 Hz, 2 H, 3(5)-H$_\alpha$], 4.91 (m, 2 H, C4=CH_2), 7.20 (m, 2 H, Ar-H$_{ortho}$), 7.38 (m, 1 H, Ar-H$_{para}$), 7.44 (m, 2 H, Ar-H$_{meta}$) ppm. ^{13}C NMR (75.4 MHz): δ = 25.0 [CH_2, C-8(9)], 37.7 (CH_2, C-10), 41.8 [CH_2, C-3(5)], 44.0 [CH, C-1(7)], 63.4 [C, C-2(6)], 109.3 (CH_2, C-4=*C*H$_2$), 126.7 (CH, Ar-C$_{ortho}$), 128.7 (CH, Ar-C$_{para}$), 129.1 (CH, Ar-C$_{meta}$), 131.8 (C, Ar-C$_{ipso}$), 146.8 (C, C-4), 179.9 (C, CON) ppm. $C_{19}H_{19}NO_2$ (293.37): calcd. C 77.79, H 6.53, N 4.77; found C 77.69, H 6.54, N 4.69.

***N*-(*p*-Methoxybenzyl)-3,7-dioxo-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (3a):** Through a cold (–78 °C) solution of **7a** (1.03 g, 3.19 mmol) in AcOEt (50 mL) a stream of ozone in oxygen (Flow 1.67 L/min, about 1.1 mmol O_3/min) was bubbled for 45 min, whereby the solution took an intense blue color. The solution was warmed to room temperature, 5% Pd/C (850 mg) was added and the mixture was subjected to hydrogenation at 1 atm and room temperature overnight. When hydrogen absorption ceased, the mixture was filtered through Celite®, washed with AcOEt (25 mL) and concentrated in vacuo to give a residue (1.15 g) which was subjected to column chromatography [silica gel (60 g), hexane/AcOEt mixtures]. On elution with hexane/AcOEt, 1:1, the known[6] **3a** (846 mg, 81% yield) was isolated as a yellow solid. The analytical sample was obtained as a white solid by crystallization from AcOEt, m.p. 177.0–177.5 °C; R_f = 0.79 (hexane/AcOEt, 1:1). IR: $\tilde{\nu}$ = 1741, 1697, 1510, 1395, 1340, 1248, 1198, 1173, 1157, 1029, 792 cm^{-1}. ^{1}H NMR: δ = 2.61 (d, *J* = 20.0 Hz, 4 H) and 2.95 (d, *J* = 20.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 3.79 (s, 3 H, OCH_3), 4.62 (s, 2 H, *N*-CH_2), 6.84 [d, *J* = 8.4 Hz, 2 H, Ar-3(5)-H], 7.27 [d, *J* = 8.4 Hz, 2 H, Ar-2(6)-H] ppm. ^{13}C NMR: δ = 42.8 (CH_2, *N*-CH_2), 47.0 [CH_2, C-2(4,6,8)], 53.6 [C, C-1(5)], 55.3 (CH_3, OCH_3), 114.3 [CH, Ar-C-3(5)], 127.1 (C, Ar-C-1), 130.0 [CH, Ar-C-2(6)], 159.6 (C, Ar-C-4), 178.0 (C, CON), 210.5 [C, C-3(7)] ppm. HRMS (APCI): calcd. for [M + H]$^+$ 327.1101; found 327.1106. $C_{18}H_{17}NO_5$ (327.34): calcd. C 66.05, H 5.23, N 4.28; found C 65.81, H 5.22, N 4.24.

***N*-Methyl-3,7-dioxo-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (3b):** This compound was prepared in a similar manner to that described for **3a**. From **7b** (680 mg, 3.13 mmol), **3b** (530 mg, 77% yield) was obtained as a white solid after crystallization from AcOEt, m.p. 243–244 °C, R_f = 0.36 (hexane/AcOEt, 1:3). IR: $\tilde{\nu}$ = 2930, 1770, 1741, 1698, 1687, 1442, 1403, 1387, 1325, 1278, 1261, 1190, 1083, 1006, 815, 797, 628 cm^{-1}. ^{1}H NMR: δ = 2.67 (d, *J* = 20.4 Hz, 4 H) and 3.04 (d, *J* = 20.4 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 3.08 (s, 3 H, *N*-CH_3) ppm. ^{13}C NMR δ = 25.5 (CH_3, *N*-CH_3), 47.4 [CH_2, C-2(4,6,8)], 53.6 [C, C-1(5)], 180.0 (C, CON), 213.8 [C, C-3(7)] ppm. HRMS (APCI): calcd. for [M + H]$^+$ 222.0761; found 222.0761. $C_{11}H_{11}NO_4$ (221.21): calcd. C 59.73, H 5.01, N 6.33; found C 59.42, H 5.11, N 6.17.

***N*-Isopropyl-3,7-dioxo-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (3c):** This compound was prepared in a similar manner to that de-

scribed for **3a**. From **7c** (400 mg, 1.63 mmol), **3c** (300 mg, 74% yield) was obtained as a white solid, after crystallization from AcOEt, m.p. 228–230 °C, R_f = 0.43 (hexane/AcOEt, 1:1). IR: $\tilde{\nu}$ = 2967, 2930, 1739, 1682, 1396, 1383, 1365, 1315, 1205, 1185, 1081, 964, 821, 631 cm^{-1}. ^{1}H NMR: δ = 1.39 [d, J = 7.2 Hz, 6 H, *N*-CH(CH_3)$_2$], 2.63 (d, J = 20.0 Hz, 4 H) and 2.98 (d, J = 20.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$), 4.37 [hept, J = 7.2 Hz, 1 H, *N*-CH(CH$_3$)$_2$] ppm. ^{13}C NMR: δ = 19.1 [CH$_3$, *N*-CH(*C*H$_3$)$_2$], 44.7 [CH, *N*-*C*H(CH$_3$)$_2$], 47.1 [CH$_2$, C-2(4,6,8)], 53.3 [C, C-1(5)], 178.3 (C, CON), 210.8 [C, C-3(7)] ppm. HRMS (APCI): calcd. for [M + H]$^+$ 250.1074; found 250.1075. $C_{13}H_{15}NO_4$ (249.27): calcd. C 62.64, H 6.07, N 5.62; found C 62.77, H 6.09, N 5.53.

***N*-*tert*-Butyl-3,7-dioxo-*cis*-bicyclo[3.3.0]octane-1,5-dicarboximide (3d):** This compound was prepared in a similar manner to that described for **3a**. From **7d** (400 mg, 1.54 mmol), **3d** (250 mg, 62% yield) was obtained as a white solid. The analytical sample was prepared by crystallization from Et$_2$O/hexane, 1:1, m.p. 215–217 °C, R_f 0.18 (Et$_2$O/AcOEt, 1:1). IR: $\tilde{\nu}$ = 2972, 2930, 1742, 1696, 1457, 1400, 1367, 1340, 1307, 1262, 1184, 1137, 1046, 1017, 982, 924, 826, 797, 632 cm^{-1}. ^{1}H NMR: δ = 1.59 [s, 9 H, *N*-C(CH$_3$)$_3$], 2.61 (dm, J = 20.0 Hz, 4 H) and 2.98 (dm, J = 20.0 Hz, 4 H, 2(4,6,8)-H$_{exo}$ and 2(4,6,8)-H$_{endo}$) ppm. ^{13}C NMR: δ = 27.1 [CH$_3$, *N*-C(*C*H$_3$)$_3$], 46.3 [CH$_2$, C-2(4,6,8)], 52.4 [C, C-1(5)], 58.3 [C, *N*-*C*(CH$_3$)$_3$], 178.3 (C, CON), 210.1 [C, C-3(7)] ppm. HRMS (APCI): calcd. for [M + H]$^+$ 260.1645; found 260.1647. $C_{14}H_{17}NO_4$·0.25H_2O (267.80): calcd. C 62.79, H 6.59, N 5.23; found C 62.93, H 6.53, N 5.01.

***N*-(*p*-Methoxybenzyl)-4-oxo-*cis*-cyclopentane-1,2-dicarboximide (10a):** This compound was prepared in a similar manner to that described before for **3a**. From **6a** (299 mg, 1.10 mmol), **10a** (195 mg, 65% yield) was obtained as a pale yellow solid. The analytical sample was obtained as a white solid by crystallization from AcOEt/hexane, 5:1, m.p. 110–111 °C, R_f = 0.55 (AcOEt). IR (KBr): $\tilde{\nu}$ = 3009, 2930, 2904, 2832, 1743, 1710, 1614, 1587, 1511, 1463, 1432, 1394, 1359, 1341, 1299, 1249, 1199, 1174, 1158, 1117, 1108, 1030, 1011, 982, 915, 825, 793, 635 cm^{-1}. ^{1}H NMR: δ = 2.47 [dm, J = 20.0 Hz, 2 H, 3(5)-H$_{cis}$], 2.69 [ddm, J = 20.0, J' = 8.4 Hz, 2 H, 3(5)-H$_{trans}$], 3.43–3.46 [m, 2 H, 1(2)-H], 3.71 (s, 3 H, OCH$_3$), 4.53 (s, 2 H, *N*-CH$_2$), 6.76 [dm, J = 8.6 Hz, 2 H, Ar-3(5)-H], 7.24 [dm, J = 8.6 Hz, 2 H, Ar-2(6)-H] ppm. ^{13}C NMR: δ = 39.1 [CH$_2$, C-3(5)], 40.7 [CH, C-1(2)], 42.3 (CH$_2$, *N*-CH$_2$), 55.2 (CH$_3$, OCH$_3$), 114.1 [CH, Ar-C-3(5)], 127.6 (C, Ar-C-1), 130.3 [CH, Ar-C-2(6)], 159.4 (C, Ar-C-4), 177.8 (C, CON), 212.8 (C, C-4) ppm. $C_{15}H_{15}NO_4$ (273.29): calcd. C 65.92, H 5.53, N 5.13; found C 65.83, H 5.50, N 5.16.

***N*-Methyl-4-oxo-*cis*-cyclopentane-1,2-dicarboximide (10b):** This compound was prepared in a similar manner to that described before for **3a**. From **6b** (535 mg, 3.24 mmol), **10b** (375 mg, 69% yield) was obtained as a pale yellow solid. The analytical sample was prepared as a white solid by crystallization from AcOEt/pentane, 2:1, m.p. 115–117 °C, R_f = 0.52 (AcOEt). IR: $\tilde{\nu}$ = 2956, 2925, 1748, 1687, 1682, 1434, 1397, 1382, 1317, 1282, 1264, 1168, 1085, 1062, 1010, 960, 836, 777, 619, 602 cm^{-1}. ^{1}H NMR: δ = 2.59 [dm, J = 20.2 Hz, 2 H, 3(5)-H$_{cis}$], 2.80 [ddm, J = 20.2, J' = 11.4 Hz, 2 H, 3(5)-H$_{trans}$], 3.03 (s, 3 H, *N*-CH$_3$), 3.55–3.59 [m, 2 H, 1(2)-H] ppm. ^{13}C NMR: δ = 25.3 (CH$_3$, *N*-CH$_3$), 39.2 [CH$_2$, C-3(5)], 40.6 [CH, C-1(2)], 178.2 (C, CON), 212.7 (C, C-4) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 168.0655; found 168.0655. $C_8H_9NO_3$ (167.16): calcd. C 57.48, H 5.43, N 8.38; found C 57.48, H 5.50, N 8.14.

***N*-Isopropyl-4-oxo-*cis*-cyclopentane-1,2-dicarboximide (10c):** This compound was prepared in a similar manner to that described before for **3a**. From **6c** (250 mg, 1.29 mmol), **10c** (160 mg, 63% yield) was isolated as a pale yellow oil after column chromatography and microdistillation at 200 °C/2 Torr in a rotary microdistillation equipment. R_f = 0.28 (AcOEt). IR: $\tilde{\nu}$ = 2978, 2935, 1744, 1687, 1459, 1396, 1383, 1363, 1310, 1224, 1173, 1164, 1137, 1090, 1044, 1021, 959, 951, 855, 837, 769 cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.39 [d, J = 6.9 Hz, 6 H, *N*-CH(CH_3)$_2$], 2.56 [dm, J = 20.0 Hz, 2 H, 3(5)-H$_{cis}$], 2.78 [ddm, J = 20.0, J' = 11.4 Hz, 2 H, 3(5)-H$_{trans}$], 3.47 [m, 2 H, 1(2)-H], 4.38 [hept, J = 6.9 Hz, 1 H, *N*-CH(CH$_3$)$_2$] ppm. ^{13}C NMR (75.4 MHz): δ = 19.1 [CH$_3$, *N*-CH(*C*H$_3$)$_2$], 39.3 [CH$_2$, C-3(5)], 40.5 [CH, C-1(2)], 44.2 [CH, *N*-*C*H(CH$_3$)$_2$], 178.1 (C, CON), 212.9 (C, C-4) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 196.0968; found 196.0960. $C_{10}H_{13}NO_3$·0.25H_2O (199.72): calcd. C 60.14, H 6.81, N 7.01; found C 60.07, H 6.63, N 6.82.

***N*-*tert*-Butyl-4-oxo-*cis*-cyclopentane-1,2-dicarboximide (10d):** This compound was prepared in a similar manner to that described before for **3a**. From **6d** (525 mg, 2.53 mmol), **10d** (325 mg, 61% yield) was obtained as a pale yellow solid. The analytical sample of **10d** was prepared as a white solid by crystallization from AcOEt/hexane, 1:4, m.p. 110–111 °C, R_f = 0.69 (AcOEt). IR (KBr): $\tilde{\nu}$ = 2976, 2928, 1741, 1693, 1484, 1456, 1398, 1368, 1339, 1310, 1262, 1232, 1178, 1105, 1013, 961, 828, 801, 765 cm^{-1}. ^{1}H NMR: δ = 1.58 [s, 9 H, *N*-C(CH$_3$)$_3$], 2.56 [br. d, J = 20.0 Hz, 2 H, 3(5)-H$_{cis}$], 2.75 [ddm, J = 20.0, J' = 11.2 Hz, 2 H, 3(5)-H$_{trans}$], 3.40 [m, 2 H, 1(2)-H] ppm. ^{13}C NMR δ = 28.2 [CH$_3$, *N*-C(*C*H$_3$)$_3$], 39.6 [CH$_2$, C-3(5)], 40.8 [CH, C-1(2)], 58.7 [C, *N*-*C*(CH$_3$)$_3$], 179.1 (C, CON), 213.3 (C, C-4) ppm. HRMS (APCI): calcd. for [M + H]$^+$ 210.1125; found 210.1120. $C_{11}H_{15}NO_3$ (209.25): C, 63.14; H, 7.23; N, 6.69. Found: C, 63.17; H, 7.20; N, 6.58.

Supporting Information (see also the footnote on the first page of this article): ^{1}H NMR spectrum of $CDCl_3$ containing TMS and ^{1}H NMR spectrum of **6a** in the same solvent and under the same conditions.

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