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Tetrahedron 62 (2006) 7645–7652

# Generation and trapping of tricyclo[3.3.0.0$^{3,7}$]oct-1(5)-ene derivatives containing carbonyl functionalities

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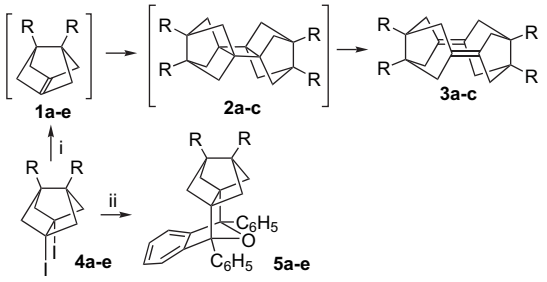
Received 11 May 2006; accepted 30 May 2006
Available online 16 June 2006

**Abstract**—Two new functionalized highly pyramidalized tricyclo[3.3.0.0$^{3,7}$]oct-1(5)-ene derivatives containing carbonyl functionalities have been trapped as Diels–Alder adducts, although they failed to dimerize. An interesting fragmentation of the bisnoradamantane skeleton to norbornane derivatives has also been observed.


## 1. Introduction

Some time ago, we published the synthesis, chemical trapping, and dimerization of two *non-functionalized* highly pyramidalized tricyclo[3.3.0.0$^{3,7}$]oct-1(5)-ene derivatives (**1a**,**b**).[1] In our continuing efforts for expanding the usefulness of pyramidalized alkenes,[2] more recently, we described the generation of *functionalized* derivatives **1c–e**. While derivatives **1c–e** were trapped as Diels–Alder adducts, only dimer **3c** was formed.[3a] Probably the sulfonyldioxy group of **1d** is not compatible with the conditions normally used to generate and dimerize highly pyramidalized alkenes (molten sodium or sodium amalgam).[3b] The lack of dimerization of **1e** is not evident because this alkene gave in medium yield a cross-coupling product with **1b** (Scheme 1).[3b]




**Scheme 1**. Reactivity of highly pyramidalized alkenes **1a–e**. **a**, R=H; **b**, R=Me; **c**, R=–OC(CH$_3$)$_2$O–; **d**, R=–OS(O)$_2$O–; **e**, R=–*o*,*o*′-biphenylene–. (i) Molten sodium, 1,4-dioxane, reflux; (ii) *t*-BuLi, 1,3-diphenylisobenzofuran, THF, −78 °C.

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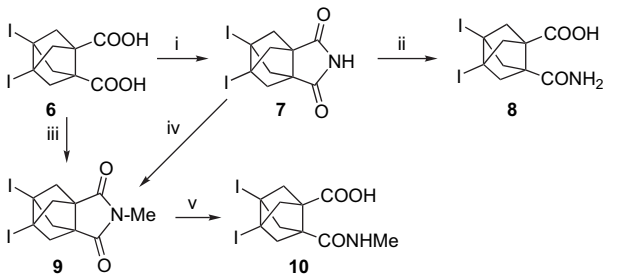
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.05.074

Owing to the rich reactivity of the carbonyl group, we considered of much interest the generation of highly pyramidalized alkenes of the type of **1** bearing carbonyl functionalities, and its possible dimerization to compounds of general structure **3**, because they may give access to new polycyclic cage compounds of theoretical interest. In this article we describe the successful generation and trapping of two new highly pyramidalized tricyclo[3.3.0.0$^{3,7}$]oct-1(5)-ene (**1f** and **1i** in Scheme 3) derivatives containing carbonyl functionalities. However, no dimers were obtained from these pyramidalized alkenes under the different reaction conditions studied. An interesting, unprecedented fragmentation of the bisnoradamantane skeleton to norbornane derivatives was observed instead when pyramidalized alkene **1i** was generated by reaction of its diiodo precursor with *t*-butyllithium (*t*-BuLi).

## 2. Results and discussion

Considering our previous experience with derivatives **1a–e**, we considered that compounds **9** and **12** could be suitable precursors for the pyramidalized alkenes **1f** and **1i**, respectively. In fact, in a related, parallel study, we had described the preparation of diester **12** and diacid **6**.[4] As shown in Scheme 2, conversion of diacid **6** into imide **9** was carried out by two alternative procedures. Reaction of diacid **6** with urea gave imide **7** in 74% yield. Alkylation of **7** with methyl iodide led to the desired *N*-methylated imide, **9** in 72% isolated yield. More conveniently, reaction of diacid **6** with acetic anhydride followed by reaction of the corresponding anhydride (not isolated) with aqueous methylamine and a second treatment with acetic anhydride led to **9** in 98% overall yield.

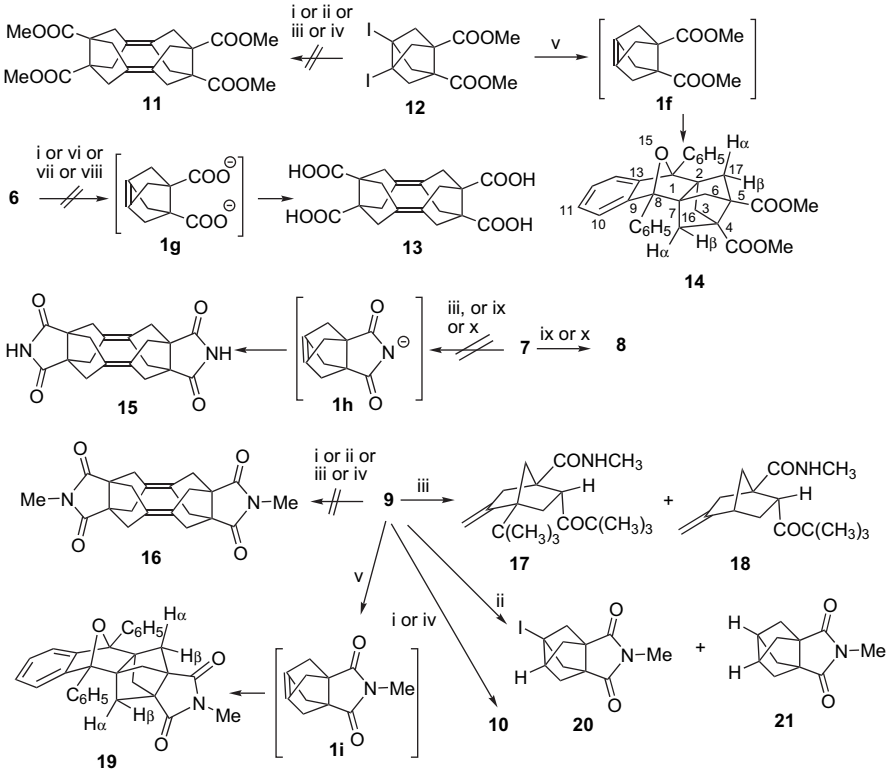


**Scheme 2**. Synthesis of the bisnoradamantane derivatives **7**–**10**. (i) Urea, 180 °C, 30 min, 74%; (ii) (a) aqueous 1 N NaOH, 50 °C, 1 h; (b) aqueous 10% HCl, 79%; (iii) (a) $Ac_2O$, reflux; (b) toluene, aqueous 40% $MeNH_2$, rt, 2.5 h; (c) $Ac_2O$, reflux, 1 h, 98%; (iv) NaH, MeI, anhydrous THF, rt, 16 h, 72%; (v) (a) aqueous 1 N NaOH, reflux, 1 h; (b) aqueous 10% HCl, 85%.

With diiodides **6**, **7**, **9**, and **12** in our hands, we first studied the generation of highly pyramidalized alkene **1f** from diester **12**. As shown in Scheme 3, reaction of **12** with *t*-BuLi in the presence of 1,3-diphenylisobenzofuran led to the isolation, in 46% yield, of **14**, presumably arising from the Diels–Alder reaction of the starting diene with the pyramidalized alkene **1f**.

Although we succeeded in generating and trapping the pyramidalized alkene **1f**, all our efforts directed toward its dimerization were fruitless. Thus, reaction of diester **12** with molten sodium in boiling 1,4-dioxane or with 0.45% Na(Hg) in 1,4-dioxane at room temperature, led to very complex mixtures of products, with important losses of material. We also used the radical anion derived from 4,4′-di-*t*-butylbiphenyl and lithium as the reducing agent[5] in this reaction but, again, a complex mixture of products, not containing the expected dimer **11**, was obtained. Taking into account that we successfully generated **1f** from **12** on reaction with *t*-butyllithium and that Borden and coworkers had previously used organolithium reagents to generate and dimerize highly pyramidalized alkenes,[6] we considered of interest to study the possible dimerization of **1f** generated by reaction of diiodide **12** with *t*-BuLi. However, owing to the well-known reactivity of these kind of highly pyramidalized alkenes with nucleophiles, a low yield of the dimer was to be expected.[7] Unfortunately, reaction of **12** with *t*-BuLi in THF at −78 °C led to a very complex mixture of products where no cyclobutane or diene dimers were detected.

Considering that the methoxycarbonyl groups were not compatible with the aggressive conditions used, we next tried the generation of highly pyramidalized alkene **1g** from diacid **6**. Unfortunately, reaction of diacid **6** with molten sodium or lithium led to the recovery of the starting material. During these reactions the formation of a precipitate was observed, so we reasoned that **6** reacted with the metal to give the disodium or dilithium salt that precipitated, thus preventing further reaction of the metals with the substrate. In order to improve the solubility we carried out the reaction of the preformed disodium salt of **6** with molten sodium in the presence of 2 equiv of the crown ether 18-crown-6.[8] However, as



**Scheme 3**. Generation and trapping of highly pyramidalized tricyclo[3.3.0.0$^{3,7}$]oct-1(5)-ene derivatives containing carbonyl functions, **1f** and **1i**. (i) Molten sodium in boiling 1,4-dioxane; (ii) 0.45% Na(Hg), 1,4-dioxane; (iii) 0.7 M *t*-BuLi in pentane, anhydrous THF, −78 °C; (iv) 4,4′-di-*t*-butylbiphenyl, Li, anhydrous THF; (v) 1,3-diphenylisobenzofuran (DPIBF), 0.7 M *t*-BuLi in pentane, anhydrous THF, −78 °C; (vi) lithium in boiling THF; (vii) preformed disodium salt of **6** plus 18-crown-6 (2 equiv) in hot 1,4-dioxane added to molten sodium in boiling 1,4-dioxane; (viii) preformed bis-tetrabutylammonium salt of **6** in 1,4-dioxane added to molten sodium in boiling 1,4-dioxane; (ix) 18-crown-6 (3 equiv) plus molten sodium in boiling 1,4-dioxane; (x) preformed sodium salt of **7** plus 18-crown-6 (3 equiv) in 1,4-dioxane added to molten sodium in boiling 1,4-dioxane.

before, a precipitate was formed, no dimers were observed, and the starting compound was mainly recovered. Similarly, when the preformed bis-tetrabutylammonium salt of **6** was reacted with molten sodium, diacid **6** was the only isolated product.

Since the solubility of disodium salts of dicarboxylic acids in 1,4-dioxane in the presence of crown ethers was low, we planned the use of the monosodium salt of imide **7** for the dimerization reaction. The preformed sodium salt of **7**, from imide **7** and NaH, was dissolved in anhydrous 1,4-dioxane in the presence of 3 equiv of 18-crown-6 and this solution was added to molten sodium in boiling 1,4-dioxane. However, the only isolated compound from this reaction was the amido acid **10**, probably formed by hydrolysis of imide **7** during the work-up. A similar result was obtained on reaction of **7** with molten sodium in boiling 1,4-dioxane in the presence of 3 equiv of 18-crown-6. The reaction of **7** with *t*-BuLi in ratios (**7**/*t*-BuLi) 1:2 or 1:3 gave complex mixtures of products where the expected cyclobutane or diene dimers were not observed.

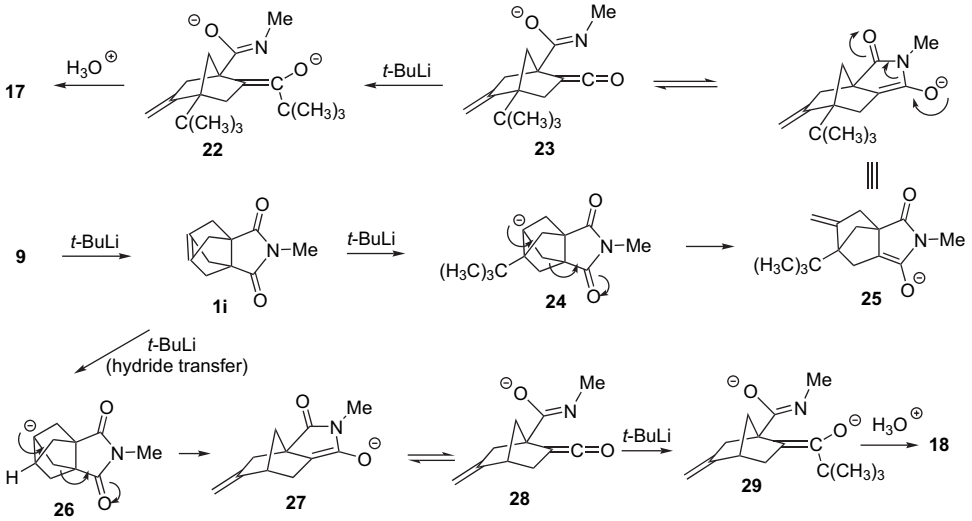
Finally, to prevent salt formation during the generation of the pyramidalized alkene we used imide **9** as the substrate, whose carbonyl functions are less reactive than the ester functions of diester **12**. Reaction of **9** with molten sodium in boiling 1,4-dioxane gave in good yield, amido acid **10** from hydrolysis of **9**, as the only detected product. A similar result was obtained when **9** was reacted with the radical anion derived from 4,4′-di-*t*-butylbiphenyl and lithium. Reaction of **9** with 0.45% sodium amalgam for 3.5 h gave a mixture containing mainly two compounds whose molecular ions in GC–MS suggest them to be the monodeiodinated and the bisdeiodinated derivatives **20** and **21**, respectively, as observed in related cases,[3b] plus a small amount of starting **9**.

However, reaction of **9** with *t*-BuLi in the presence of 1,3-diphenylisobenzofuran gave the expected compound **19**, the Diels–Alder adduct of the pyramidalized alkene **1i**, and the diene, in medium yield. Since formation of the pyramidalized alkene appeared to be possible by reaction with *t*-BuLi, we tried the reaction of **9** with *t*-BuLi in the absence of a trapping agent with the aim of favoring the dimer formation. From this reaction we obtained a complex mixture, which analyzed by GC–MS showed to contain two main components (rt, 14.84 and 17.92 min, 21 and 37% relative areas, respectively). These compounds could be isolated in low yield by column chromatography and were fully characterized by spectroscopic means, showing that they were compounds **18** (rt, 14.84 min) and **17** (rt, 17.92 min), respectively.

The formation of these compounds may be explained as shown in Scheme 4 via the intermediate formation of the pyramidalized alkene **1i**. Nucleophilic addition of *t*-BuLi to **1i** would give carbanion **24**, which could experience the shown fragmentation giving rise to the enolate **25**, containing the norbornane framework, thus releasing the strain of the tricyclo[3.3.0.0$^{3,7}$]octane skeleton. Enolate **25** might be in equilibrium with the ketene anion **23**, which on reaction with *t*-BuLi could give dianion **22**. Protonation of this dianion during the quenching of the reaction mixture would give **17**, in which the *endo*-arrangement of the pivaloyl group could be due to the kinetically controlled protonation of the corresponding ketone enolate by the less hindered *exo*-side. In a similar way, *t*-BuLi could transfer a hydride to the pyramidalized alkene **1i**, the formed anion **26** could rearrange to enolate **27**, which might be in equilibrium with ketene anion **28**. Addition of *t*-BuLi to the ketene function as before would give dianion **29**, which, on protonation, would give **18** with the pivaloyl group in an *endo*-arrangement, as for **17**.

All of the new compounds herein described were fully characterized by spectroscopic means (IR, $^{1}$H and $^{13}$C NMR, MS) and elemental analysis or accurate mass measurement. Assignments given for the NMR spectra are based on DEPT, COSY $^{1}$H/$^{1}$H, HETCOR $^{1}$H/$^{13}$C (HSQC and HMBC sequences for one bond and long range heterocorrelations, respectively), and NOESY experiments for selected compounds.

Also, we have performed DFT calculations [B3LYP/6-31G(d)] on pyramidalized alkenes **1f** and **1i** (Fig. 1). All




**Scheme 4**. Possible mechanisms for the formation of compounds **17** and **18** in the reaction of **9** with *t*-BuLi.

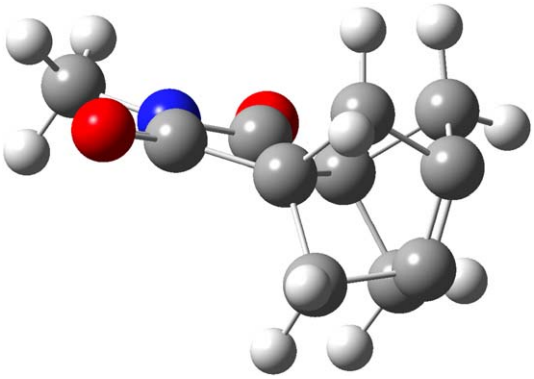


**Figure 1**. Minimum energy conformation [B3LYP/6-31G(d)] of highly pyramidalized alkene **1i**.

the calculated parameters compare very well with those previously calculated for related pyramidalized alkenes. Thus, the pyramidalization angles of **1f** and **1i** ($\Phi$=61.5 and 61.7°, respectively) and the carbon–carbon double bond length (1.380 and 1.381 Å, respectively) are quite similar to those previously calculated for **1a–e**.[2a] Also, the distance between the α-ester carbon atoms in diester **1f** (1.703 Å) is comparable to that previously calculated between the methyl-bearing carbon atoms in **1b** (1.704 Å). In the pyramidalized alkene **1i**, the distance between the α-carbonyl carbon atoms is shorter (1.636 Å) as in the related cases **1c** (1.625 Å) or **1d** (1.645 Å), where the substituents on C1 and C5 are connected through a five-membered ring.

## 3. Conclusions

In conclusion, two new highly pyramidalized alkenes containing carbonyl groups (**1f** and **1i**) have been generated and trapped as Diels–Alder adducts. Several attempts to carry out the dimerization of these alkenes were unsuccessful, probably due in part to the lability of the carbonyl groups. We failed to generate the pyramidalized alkenes **1g** and **1h**, derived from diacid **6** and imide **7**, respectively, probably due to the formation of insoluble salts under the reaction conditions, in spite of using 18-crown-6 to increase the solubility of these salts. Interestingly, the reaction of the *N*-methylated imide **9** with *t*-BuLi led to a mixture of two norbornane derivatives as a result of an unprecedented anion-induced fragmentation of the bisnoradamantane skeleton followed by reaction of *t*-BuLi with the intermediate ketene, thus formed, and protonation of the enolate from the less hindered exo face during the work up.

## 4. Computational details

All quantum-mechanical calculations were carried out at Becke's three-parameter hybrid functional with the Lee, Yang, and Parr correlation functional (B3LYP) level,[9] using the 6-31G(d) basis set,[10] as implemented in Gaussian 03 on a Compaq HPC320 computer.[11] Geometry optimizations were undertaken using appropriate symmetry constraints and default convergence limits. The minimum energy nature of the optimized structures was verified from vibrational frequency analysis.

## 5. Experimental

### 5.1. General

Melting points were determined with a MFB 595010 M Gallenkamp melting point apparatus. Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in the following spectrometers: $^1$H NMR (500 MHz, Varian VXR 500), $^{13}$C NMR (75.4 MHz, Varian Gemini 300). $^1$H and $^{13}$C NMR chemical shifts ($\delta$) are reported in parts per million with respect to internal tetramethylsilane (TMS). The multiplicity of the signals is: s, singlet; d, doublet; t, triplet, q, quartet, m, multiplet; or their combinations. Assignments given for the NMR spectra are based on DEPT, COSY $^1$H/$^1$H, HETCOR $^1$H/$^{13}$C (HSQC and HMBC sequences for one bond and long range heterocorrelations, respectively), and NOESY experiments for selected compounds. Diastereotopic methylene protons in tricyclo[3.3.0.0$^{3,7}$]octane derivatives are referred as $H_\alpha$/$H_\beta$ as shown in the corresponding structures. IR spectra were recorded on a FT/IR Perkin–Elmer spectrometer, model 1600; only the more intense absorption bands are given. Routine MS spectra were taken on a Hewlett–Packard 5988A spectrometer, the sample was introduced directly or through a gas chromatograph, Hewlett–Packard model 5890 Series II, equipped with a 30-meter HP-5 (5% diphenyl/95% dimethyl-polysiloxane) column [conditions: 10 psi, initial temperature: 35 °C (2 min), then heating at a rate of 8 °C/min then isothermic at 300 °C] and the electron impact technique (70 eV). Only significant ions are given: those with higher relative abundance, except for the ions with higher *m*/*z* values. HRMS were performed on a Micromass Autospec spectrometer. Neutral aluminum oxide (MN), Brockmann activity 1 or silica gel SDS 60 (35–70 μm) was utilized for the standard and flash column chromatography, respectively. NMR and routine MS spectra were performed at the *Serveis Científico-Tècnics* of the University of Barcelona, while high resolution mass spectra and elemental analyses were carried out at the Mass Spectrometry Laboratory of the University of Santiago de Compostela (Spain) and at the Microanalysis Service of the IIQAB (C.S.I.C, Barcelona, Spain), respectively.

### 5.2. 3,7-Diiodotricyclo[3.3.0.0$^{3,7}$]octane-1,5-dicarboximide (7)

A mixture of diacid **6** (237 mg, 0.53 mmol) and urea (160 mg, 2.64 mmol) was melted at about 130 °C and then heated to 180 °C for 30 min. The black residue was taken in water (20 mL) and the mixture was extracted with diethyl ether (6×10 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to dryness to give imide **7** (167 mg, 74% yield) as a white solid. The analytical sample was obtained by crystallization from diethyl ether, mp>219 °C (dec). IR (KBr): $\nu$ 3400–2700 (max. at 3200, 3074, 2996, 2946), 1768 and 1706 (C=O, st), 1475, 1381, 1341, 1311, 1273, 1143, 1097, 1069, 1055, 961, 835, 775, 731, 707, 617 cm$^{-1}$. $^1$H NMR (300 MHz): $\delta$ 2.42 (d, $J$=8.0 Hz, 4H) and 2.68 (d, $J$=8.0 Hz, 4H) [2(4,6,8)-$H_\alpha$ and 2(4,6,8)-$H_\beta$], 7.60–7.80 (br s, 1H, NH). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2.50 [s, 8H, 2(4,6,8)-$H_\alpha$ and 2(4,6,8)-$H_\beta$], 11.15 (1H, NH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 44.0 [C, C3(7)], 58.5 [C, C1(5)], 58.8 [$CH_2$, C2(4,6,8)], 173.4 (C, imide CO). MS (EI), *m*/*z* (%): 429 ($M^{\bullet+}$, 2), 358

[(M−CONHCO)$^{\bullet+}$, 2], 302 [(M−I)$^+$, 8], 259 [(M−I−CONH)$^+$, 10], 231 [(M−I−CONHCO)$^+$, 97], 105 (12), 104 [(M−2I−CONHCO)$^+$, 100], 103 (33), 78 (28), 77 (30), 63 (20). MS (ESI−), *m/z* (%): 429 (9), 428 [(M−H)$^-$, 100]. Accurate mass measurement: calcd for $C_{10}H_8I_2NO_2$ [(M−H)$^-$]: 427.8639; found: 427.8647.

### 5.3. 5-Carbamoyl-3,7-diiodotricyclo[3.3.0.0$^{3,7}$]octane-1-carboxylic acid (8)

A mixture of imide **7** (89 mg, 0.21 mmol) and aqueous 1 N NaOH (0.75 mL) was heated at about 50 °C for 1 h. The obtained solution was diluted with water (2 mL) and made acidic with aqueous 10% HCl (1 mL). The precipitated solid was filtered in vacuo, thoroughly washed with water, and dried in vacuo in the presence of $P_2O_5$ to give amide acid **8** (74 mg, 79% yield) as a white solid, mp>236 °C (dec). IR (KBr): $\nu$ 3500–2150 (max. at 3477, 3344, 3000, 2925, 2581), 1702 and 1630 (C=O, st), 1594, 1477, 1406, 1310, 1276, 1238, 1216, 1172, 1097, 994, 963 cm$^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2.28–2.42 (complex signal, 8H, 2(8)-$H_2$ and 4(6)-$H_2$], 7.10 (s, 1H) and 7.14 (s, 1H, $CONH_2$), 12.48 (br s, 1H, COOH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 42.9 [C, C3(7)], 58.0 (C) and 59.9 [C, (C1 and C5)], 60.7 ($CH_2$) and 60.8 ($CH_2$) [C2(8) and C4(6)], 169.5 (C, $CONH_2$), 170.1 (C, COOH). MS (EI), *m/z* (%): 447 (M$^{\bullet+}$, 1), 430 [(M−OH)$^+$, 1], 320 [(M−I)$^+$, 7], 302 [(M−I−$H_2O$)$^+$, 9], 280 (57), 262 (11), 231 (20), 153 (60), 148 (21), 147 (21), 136 (22), 135 (27), 127 (17), 105 (42), 104 (90), 103 (77), 78 (53), 77 (100), 65 (34), 63 (37), 51 (75). MS (ESI−), *m/z* (%): 915 [(2M−2H+Na)$^-$, 15]. 447 (15), 446 [(M−H)$^-$, 100], 402 [(M−H−$CO_2$)$^-$, 36]. Accurate mass measurement: calcd for $C_{10}H_{10}I_2NO_3$ [(M−H)$^-$]: 445.8745; found: 445.8742.

### 5.4. 3,7-Diiodo-*N*-methyltricyclo[3.3.0.0$^{3,7}$]octane-1,5-dicarboximide (9)

**5.4.1. From diacid 6.** A mixture of diacid **6** (100 mg, 0.22 mmol) and acetic anhydride (2 mL) was heated under reflux for 1 h. The excess acetic anhydride and the formed acetic acid were distilled off in vacuo and the residue (97 mg) was dissolved in toluene (0.5 mL), 40% aqueous methylamine solution (20 μL, 0.24 mmol) was added and the mixture stirred for 2.5 h at room temperature. Concentration of the mixture in vacuo gave a yellowish residue (111 mg), acetic anhydride (2 mL) was added and the mixture was heated under reflux for 1 h. Evaporation of the volatile compounds in vacuo gave a yellowish residue (108 mg), which was submitted to column chromatography [neutral aluminum oxide (1.2 g), heptane/ethyl acetate mixtures]. On elution with a mixture heptane/ethyl acetate in the ratio of 9:1, imide **9** was obtained as a white solid (97 mg, 98% global yield). The analytical sample was obtained by crystallization from ethyl acetate/*n*-pentane (1:1), mp 176–177 °C. IR (KBr): $\nu$ 2995, 2946, 2907, 1764 and 1699 (C=O, st), 1419, 1372, 1318, 1266, 1126, 1114, 1012, 964, 836, 795, 735 cm$^{-1}$. $^1$H NMR (300 MHz): $\delta$ 2.34 (d, $J$=8.1 Hz, 4H) and 2.69 (d, $J$=8.1 Hz, 4H) [2(4,6,8)-$H_\alpha$ and 2(4,6,8)-$H_\beta$], 3.01 (s, 3H, N-$CH_3$). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.3 ($CH_3$, N-$CH_3$), 42.1 [C, C3(7)], 57.8 [C, C1(5)], 60.1 [$CH_2$, C2(4,6,8)], 171.8 (C, imide CO). MS (EI), *m/z* (%): 443 (M$^{\bullet+}$, 2), 316 [(M−I)$^+$, 39], 231 [(M−I−CONMeCO)$^+$, 85], 132 (11), 105 (10), 104 [(M−2I−CONMeCO)$^{\bullet+}$, 100], 103 (20). Elemental analysis: calcd for $C_{11}H_{11}I_2NO_2$ (443.02): C 29.82, H 2.50, N 3.16, I 57.29. Found: C 29.88, H 2.32, N 3.13, I 56.95.

**5.4.2. From imide 7.** A mixture of imide **7** (160 mg, 0.37 mmol) and NaH (24 mg of a 45–55% suspension in mineral oil, about 0.5 mmol) in anhydrous THF (2 mL) was magnetically stirred under an argon atmosphere for 30 min. Then, methyl iodide (0.4 mL, 0.91 g, 6.4 mmol) was added and the mixture was stirred for 1 h. More methyl iodide (0.4 mL, 6.4 mmol) was added and the mixture was stirred for 15 h more. The reaction mixture was concentrated in vacuo and the solid residue was extracted with $CH_2Cl_2$ (3×10 mL). The combined organic extracts were filtered and concentrated in vacuo to give imide **9** (119 mg, 72% yield) as a yellowish solid.

### 5.5. 3,7-Diiodo-5-(*N*-methylcarbamoyl)tricyclo[3.3.0.0$^{3,7}$]-octane-1-carboxylic acid (10)

A mixture of imide **9** (100 mg, 0.23 mmol) and aqueous 0.5 N NaOH (0.7 mL) was heated under reflux for 1 h. The obtained solution was diluted with water (2 mL) and made acidic with aqueous 10% HCl. The precipitated solid was filtered in vacuo, thoroughly washed with water and dried in vacuo in the presence of $P_2O_5$ to give amide acid **10** (88 mg, 85% yield) as a white solid, mp 223.5–226 °C (dec). IR (KBr): $\nu$ 3400–2200 (max. at 3373, 2943, 2624), 1696 and 1627 (C=O, st), 1612, 1549, 1474, 1420, 1330, 1292, 1248, 1219, 1160, 1110, 1072, 991, 960, 743, 710, 640 cm$^{-1}$. $^1$H NMR (300 MHz, $CD_3OD$): $\delta$ 2.39–2.49 (complex signal, 8H, 2(8)-$H_2$ and 4(6)-$H_2$], 2.70 (s, 3H, $NHCH_3$), 4.85 (s, mobile H, COOH and CONHMe). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 26.1 ($CH_3$, $NHCH_3$), 42.8 [C, C3(7)], 58.2 (C) and 60.0 [C, C1 and C5], 60.6 ($CH_2$) and 60.7 [$CH_2$, C2(8) and C4(6)], 167.9 (C, CON), 170.1 (C, COOH). MS (EI), *m/z* (%): 461 (M$^{\bullet+}$, 1), 443 [(M−$H_2O$)$^{\bullet+}$, 1], 334 [(M−I)$^+$, 14], 316 [(M−I−$H_2O$)$^+$, 44], 294 (97), 231 [(M−I−CONHMe−COOH)$^+$, 83], 167 (97), 149 (77), 127 (23), 105 (35), 104 [(M−2I−CONHMe−COOH)$^{\bullet+}$, 100], 103 (57), 78 (21), 77 (35). Elemental analysis: calcd for $C_{11}H_{13}I_2NO_3$ (461.04): C 28.66, H 2.84, N 3.04, I 55.05. Found: C 28.95, H 2.64, N 2.83, I 55.02.

### 5.6. Reaction of the sodium salt of imide 7 with molten sodium in boiling 1,4-dioxane in the presence of 18-crown-6

A solution of imide **7** (100 mg, 0.23 mmol) in anhydrous 1,4-dioxane (1.5 mL) was added to a suspension of NaH (9 mg, 55–65% in mineral oil, 0.23 mmol, previously washed with the above solvent) in the same solvent (1 mL), and the mixture was heated under reflux for 10 min, with formation of a white precipitate. Then, 18-crown-6 (186 mg, 0.7 mmol) was added until the precipitate was completely dissolved. The above solution was added to molten sodium (54 mg, 2.4 mmol) in boiling 1,4-dioxane (1 mL) and the mixture was heated under reflux for 3 h under an argon atmosphere. The mixture was allowed to cool to room temperature and was filtered by washing the solid with diethyl ether (3×10 mL). The combined filtrate and washings were concentrated to dryness in vacuo to give a solid residue (145 mg), which showed to be mainly 18-crown-6 ($^1$H NMR). The excess sodium from the

filter was destroyed by careful addition to water, and then the filter was washed with more water (10 mL). The combined aqueous phases were made acidic with 2 N HCl and were extracted with AcOEt (3×10 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$), filtered, and concentrated to dryness in vacuo to give a solid residue (59 mg), which showed to be **8** ($^1$H NMR).

### 5.7. Dimethyl 1,8-diphenyl-15-oxahexacyclo-[6.6.1.1$^{2,5}$.1$^{4,7}$.0$^{2,7}$.0$^{9,14}$]heptadeca-9,11,13-triene-4,5-dicarboxylate (14)

To a cold (−78 °C) solution of diiodide **12** (100 mg, 0.21 mmol) and 1,3-diphenylisobenzofuran (DPIBF, 63 mg, 0.23 mmol) in anhydrous THF (3.2 mL) under an argon atmosphere, a solution of *t*-BuLi (1.5 M in *n*-pentane, 0.3 mL, 0.45 mmol) was added dropwise. After 30 min at −78 °C, the mixture was allowed to heat to room temperature, methanol (1.3 mL) and water (4 mL) were added and it was extracted with diethyl ether (3×5 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a yellowish solid (114 mg), which was submitted to column chromatography [neutral aluminum oxide (11 g), column diameter: 1.5 cm, hexane/AcOEt mixtures]. On elution with a mixture hexane/AcOEt in the ratio of 96:4, compound **14** (47 mg, 46% yield) was isolated. An analytical sample of **14** (21 mg, 21% yield) was obtained as a white crystalline solid, mp 220–221 °C, by crystallization of the above product from diethyl ether (4.5 mL). IR (KBr): $\nu$ 3025, 2983, 2942, 2891, 1731 (C=O, st), 1603, 1477, 1457, 1448, 1432, 1351, 1302, 1272, 1236, 1217, 1186, 1113, 979, 765, 744, 734, 699, 660 cm$^{-1}$. $^1$H NMR: $\delta$ 1.34 [dd, $J$=8.5 Hz, $J'$=3.5 Hz, 2H, 3(16)-H$_\beta$], 1.92 [dd, $J$=8.5 Hz, $J'$=3.5 Hz, 2H, 6(17)-H$_\beta$], 2.06 [d, $J$=8.5 Hz, 2H, 6(17)-H$_\alpha$], 2.22 [d, $J$=8.5 Hz, 2H, 3(16)-H$_\alpha$], 3.57 (s, 3H, 5COOCH$_3$), 3.60 (s, 3H, 4COOCH$_3$), 6.98 [m, 2H, 10(13)-H], 7.11 [m, 2H, 11(12)-H], 7.36 (tt, $J$=7.5 Hz, $J'$=1.5 Hz, 2H, ArH$_{para}$), 7.44 (m, 4H, ArH$_{meta}$), 7.58 (m, 4H, ArH$_{ortho}$). $^{13}$C NMR: $\delta$ 50.0 [CH$_2$, C3(16)], 50.1 [CH$_2$, C6(17)], 51.69 [CH$_3$, 5COO*C*H$_3$)], 51.75 [CH$_3$, 4COO*C*H$_3$)], 60.6 (C, C4), 61.1 (C, C5), 66.4 [C, C2(7)], 87.5 [C, C1(8)], 120.2 [CH, C10(13)], 125.6 (CH, ArC$_{ortho}$), 127.0 [CH, C11(12)], 127.8 (CH, ArC$_{para}$), 128.5 (CH, ArC$_{meta}$), 137.1 (C, ArC$_{ipso}$), 147.2 [C, C9(14)], 171.6 [C, C4*C*OOCH$_3$)], 171.7 [C, C5*C*OOCH$_3$)]. MS (EI), *m*/*z* (%): 492 (M$^{\bullet+}$, 10), 388 (25), 387 (94), 271 (25), 270 [(C$_{20}$H$_{14}$O)$^{\bullet+}$, 59], 241 (24), 239 (20), 165 (25), 105 (C$_6$H$_5$CO$^+$, 100), 103 (39), 77 (83), 59 (60). Elemental analysis: calcd for C$_{32}$H$_{28}$O$_5$·0.4H$_2$O (499.78): C 76.90, H 5.81. Found: C 76.69, H 5.71.

### 5.8. Reaction of imide 7 with molten sodium in boiling 1,4-dioxane in the presence of 18-crown-6

Solid imide **7** (155 mg, 0.36 mmol) was added to molten sodium (83 mg, 3.6 mmol) in a boiling solution of 18-crown-6 (289 mg, 1.09 mmol) in 1,4-dioxane (3.6 mL) and the mixture was heated under reflux for 2.5 h under an argon atmosphere. The mixture was allowed to cool to room temperature and was filtered by washing the solid with diethyl ether (3×10 mL). The combined filtrate and washings were concentrated to dryness in vacuo to give a brown oily residue (318 mg), which showed to be mainly the crown ether. The sodium from the filter was destroyed by careful addition to water, then the filter was washed with water (5 mL), and the combined aqueous phases were made acidic with 2 N HCl and were extracted with AcOEt (3×10 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a yellowish solid residue (65 mg) which, after being washed with *n*-pentane (3×0.5 mL) and $CH_2Cl_2$ (3×0.2 mL), gave amide acid **8** (58 mg, 36%).

### 5.9. Reaction of imide 9 with *t*-butyllithium: 4-*t*-butyl-*endo*-2-(2,2-dimethylpropionyl)-*N*-methyl-5-methylenebicyclo[2.2.1]heptane-1-carboxamide (17) and *endo*-2-(2,2-dimethylpropionyl)-*N*-methyl-5-methylenebicyclo-[2.2.1]heptane-1-carboxamide (18)

To a cold (−78 °C) solution of diiodide **9** (100 mg, 0.23 mmol) in anhydrous THF (1.2 mL), kept under an argon atmosphere, a solution of *t*-BuLi (0.7 M in *n*-pentane, 0.6 mL, 0.42 mmol) was added dropwise. After 45 min at −78 °C, the mixture was allowed to heat to room temperature, methanol (0.4 mL) and water (2 mL) were added and the mixture was extracted with diethyl ether (4×5 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a residue (34 mg), which was analyzed by GC–MS showing the presence of two main components, **18** (rt 14.84 min, 21% relative area, molecular ion *m*/*z*=249) and **17** (rt 17.92 min, 37% relative area, molecular ion *m*/*z*=305), the rest of components showing relative areas below 6%. The above residue was submitted to column chromatography [flash silica gel (3.4 g), column diameter: 1 cm, heptane/AcOEt mixtures in ratios from 6:4 to 4:6]. In order of elution, slightly impure compound **17** (7 mg) and pure **18** (8 mg, 14% yield) were isolated as colorless oils.

When this reaction was carried out as before but using 0.21 mmol *t*-BuLi, instead of 0.42 mmol, a residue (37 mg) containing mainly **18** (17% relative area), **17** (50% relative area), and other components showing relative areas below 10%, was obtained. Column chromatography of the above residue [flash silica gel (6 g), column diameter: 1 cm, heptane/AcOEt mixtures] allowed us to isolate pure **17** (8 mg, 11% yield) as a colorless oil. Spectroscopic and analytic data of **17**: IR (KBr): $\nu$ 3409, 3088, 2970, 2871, 1693 and 1661 (C=O, st), 1533, 1478, 1464, 1412, 1366, 1092, 1078, 894 cm$^{-1}$; $^1$H NMR: $\delta$ 1.07 [s, 9H, 4-C(C*H*$_3$)$_3$], 1.09 [s, 9H, 2-COC(C*H*$_3$)$_3$], 1.36 (ddd, $J_{3\text{-H}_{endo}/3\text{-H}_{exo}}$=12.0 Hz, $J_{2\text{-H}/3\text{-H}_{endo}}$=7.0 Hz, $J_{3\text{-H}_{endo}/7\text{-H}_{anti}}$=2.5 Hz, 1H, 3-H$_{endo}$), 1.69 (dd, $J_{7\text{-H}_{anti}/7\text{-H}_{syn}}$=10.0 Hz, $J_{3\text{-H}_{endo}/7\text{-H}_{anti}}$=2.5 Hz, 1H, 7-H$_{anti}$), 1.95 (ddd, $J_{7\text{-H}_{anti}/7\text{-H}_{syn}}$=10.0 Hz, $J_{6\text{-H}_{endo}/7\text{-H}_{syn}}$= 2.0 Hz, 1H, 7-H$_{syn}$), 2.33 (t, $J_{3\text{-H}_{endo}/3\text{-H}_{exo}}$=12.0 Hz, $J_{2\text{-H}/3\text{-H}_{exo}}$=12.0 Hz, 1H, 3-H$_{exo}$), 2.37 (dq, $J_{6\text{-H}_{exo}/6\text{-H}_{endo}}$= 15.0 Hz, $J_{2\text{-H}/6\text{-H}_{exo}}$=2.0 Hz, $J_{6\text{-H}_{exo}/5=\text{CH}(Z)}$=2.0 Hz, $J_{6\text{-H}_{exo}/5=\text{CH}(E)}$=2.0 Hz, 1H, 6-H$_{exo}$), 2.75 (d, $J_{\text{NH}/\text{NHC}H_3}$= 5.0 Hz, 3H, NHC*H*$_3$), 3.45 (ddt, $J_{6\text{-H}_{exo}/6\text{-H}_{endo}}$=15.0 Hz, $J_{6\text{-H}_{endo}/7\text{-H}_{syn}}$=2.0 Hz, $J_{6\text{-H}_{endo}/5=\text{CH}(Z)}$=3.0 Hz, $J_{6\text{-H}_{endo}/5=\text{CH}(E)}$= 2.0 Hz, 1H, 6-H$_{endo}$), 3.59 (ddd, $J_{2\text{-H}/3\text{-H}_{exo}}$=12.0 Hz, $J_{2\text{-H}/3\text{-H}_{endo}}$=7.0 Hz, $J_{2\text{-H}/6\text{-H}_{exo}}$=2.0 Hz, 1H, 2-H), 4.84 (t, $J_{5=\text{CH}(E)/6\text{-H}_{exo}}$=2.0 Hz, $J_{5=\text{CH}(E)/6\text{-H}_{endo}}$=2.0 Hz, 1H, 5=CH(*E*)), 4.97 (t, $J_{5=\text{CH}(Z)/6\text{-H}_{exo}}$=2.0 Hz, $J_{5=\text{CH}(Z)/6\text{-H}_{endo}}$= 3.0 Hz, 1H, 5=CH(*Z*)), 5.66 (br s, 1H, N*H*CH$_3$). $^{13}$C NMR (100.6 MHz): $\delta$ 26.0 [CH$_3$, 2-COC(*C*H$_3$)$_3$], 26.2 (CH$_3$,

NH*C*H$_3$), 27.2 [CH$_3$, 4-C(*C*H$_3$)$_3$], 32.4 [C, 4-*C*(CH$_3$)$_3$], 37.7 (CH$_2$, C3), 38.3 (CH$_2$, C6), 44.8 [C, 2-CO*C*(CH$_3$)$_3$], 45.8 (CH$_2$, C7), 49.3 (CH, C2), 55.0 (C, C1), 60.6 (C, C4), 104.4 (CH$_2$, 5=CH$_2$), 152.4 (C, C5), 174.1 (C, *C*ONHMe), 218.8 [C, 2-*C*OC(CH$_3$)$_3$]. MS (EI), *m/z* (%): 305 (M$^{\bullet+}$, 3), 248 [(M−*t*-Bu)$^+$, 31], 193 (8), 164 [(M−*t*-BuCO)$^+$, 9], 136 (40), 58 (29), 57 (100). MS (ESI+), *m/z* (%): 634 (19), 633 [(2M+Na)$^+$, 30], 344 [(M+K)$^+$, 10], 329 (31), 328 [(M+Na)$^+$, 100], 325 (13), 306 [(M+H)$^+$, 32], 275 [(M−NHCH$_3$)$^+$, 22]. Accurate mass measurement (ESI+): calcd for $C_{19}H_{32}NO_2$ [(M+H)$^+$]: 306.2428; found: 306.2424. Spectroscopic and analytic data of **18**: IR (KBr): $\nu$ 3343, 3072, 2963, 2872, 1698, 1643 (C=O, st), 1538, 1479, 1467, 1409, 1366, 1270, 1086, 902, 873 cm$^{-1}$. $^1$H NMR: $\delta$ 1.09 [s, 9H, 2-COC(C*H*$_3$)$_3$], 1.38 (ddd, $J_{3\text{-H}_{endo}/3\text{-H}_{exo}}$= 12.0 Hz, $J_{2\text{-H}/3\text{-H}_{endo}}$=6.0 Hz, $J_{3\text{-H}_{endo}/7\text{-H}_{anti}}$=2.0 Hz, 1H, 3-H$_{endo}$), 1.71 (dt, $J_{7\text{-H}_{anti}/7\text{-H}_{syn}}$=10.0 Hz, $J_{3\text{-H}_{endo}/7\text{-H}_{anti}}$=2.0 Hz, $J_{4\text{-H}/7\text{-H}_{anti}}$=2.0 Hz, 1H, 7-H$_{anti}$), 1.93 (ddd, $J_{7\text{-H}_{anti}/7\text{-H}_{syn}}$= 10.0 Hz, $J_{6\text{-H}_{endo}/7\text{-H}_{syn}}$=3.0 Hz, $J_{4\text{-H}/7\text{-H}_{syn}}$=2.0 Hz, 1H, 7-H$_{syn}$), 2.24 (dt, $J_{3\text{-H}_{endo}/3\text{-H}_{exo}}$=12.0 Hz, $J_{2\text{-H}/3\text{-H}_{exo}}$=12.0 Hz, $J_{3\text{-H}_{exo}/4\text{-H}}$=5.0 Hz, 1H, 3-H$_{exo}$), 2.25 (dm, $J_{6\text{-H}_{exo}/6\text{-H}_{endo}}$= 15.0 Hz, 1H, 6-H$_{exo}$), 2.77 (d, $J_{\text{NH/NHC}H_3}$=5.0 Hz, 3H, NHC*H*$_3$), 2.81 (br d, $J_{3\text{-H}_{exo}/4\text{-H}}$=5.0 Hz, 1H, 4-H), 3.37 (ddt, $J_{6\text{-H}_{exo}/6\text{-H}_{endo}}$=15.0 Hz, $J_{6\text{-H}_{endo}/7\text{-H}_{syn}}$=2.0 Hz, $J_{6\text{-H}_{endo}/5=\text{CH}(Z)}$= 2.0 Hz, $J_{6\text{-H}_{endo}/5=\text{CH}(E)}$=3.0 Hz, 1H, 6-H$_{endo}$), 3.55 (ddd, $J_{2\text{-H}/3\text{-H}_{exo}}$=12.0 Hz, $J_{2\text{-H}/3\text{-H}_{endo}}$=6.0 Hz, $J_{2\text{-H}/6\text{-H}_{exo}}$=2.0 Hz, 1H, 2-H), 4.65 (br s, 1H, 5=C*H*(*E*), 4.84 (t, $J_{5=\text{CH}(Z)/6\text{-H}_{exo}}$= 2.0 Hz, $J_{5=\text{CH}(Z)/6\text{-H}_{endo}}$=2.0 Hz, 1H, 5=CH(*Z*)), 5.72 (br s, 1H, N*H*CH$_3$). $^{13}$C NMR (100.6 MHz): $\delta$ 26.1 [CH$_3$, 2-COC(*C*H$_3$)$_3$], 26.3 (CH$_3$, NHC*H*$_3$), 34.4 (CH$_2$, C6), 36.5 (CH$_2$, C3), 44.4 (CH$_2$, C7), 44.8 [C, 2-CO*C*(CH$_3$)$_3$], 46.4 (CH, C4), 48.5 (CH, C2), 57.9 (C, C1), 102.7 (CH$_2$, 5=CH$_2$), 152.7 (C, C5), 174.1 (C, *C*ONHMe), 219.0 [C, 2-*C*OC(CH$_3$)$_3$]. MS (EI), *m/z* (%): 249 (M$^{\bullet+}$, 19), 192 [(M−*t*-Bu)$^+$, 20], 164 [(M−*t*-BuCO)$^+$, 18], 137 (63), 107 (18), 105 (21), 91 (20), 86 (20), 79 (31), 77 (25), 58 (77), 57 (100). MS (ESI+), *m/z* (%): 273 (17), 272 [(M+Na)$^+$, 100], 250 [(M+H)$^+$, 4]. Accurate mass measurement (ESI+): calcd for $C_{15}H_{24}NO_2$ [(M+H)$^+$]: 250.1802; found: 250.1797.

### 5.10. Reaction of imide 9 with molten sodium in boiling 1,4-dioxane

Solid imide **9** (100 mg, 0.23 mmol) was added to molten sodium (52 mg, 2.25 mmol) in boiling 1,4-dioxane (2.2 mL) and the mixture was heated under reflux for 4 h under an argon atmosphere. The mixture was allowed to cool to room temperature and was filtered by washing the solid with diethyl ether (3×10 mL) and 1,4-dioxane (10 mL). The combined filtrate and washings were concentrated to dryness in vacuo to give a solid residue (52 mg), which showed to be partially insoluble in $CD_3OD$. This solid was taken in water (5 mL), acidified with 2 N HCl, and extracted with AcOEt (3×10 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a solid residue (16 mg), which showed to be amide acid **10**. The sodium from the filter was destroyed by careful addition to water, and then the filter was washed with water (5 mL). The combined aqueous phases were made acidic with 2 N HCl and were extracted with AcOEt (3×6 mL). The combined organic extracts were treated as before to give more **10** (83 mg, total yield 95%).

### 5.11. Reaction of imide 9 with the radical anion from lithium and 4,4′-di-*t*-butylbiphenyl

A solution of 4,4′-di-*t*-butylbiphenyl (141 mg, 0.53 mmol) in anhydrous THF (1.5 mL) was placed in a Schlenk tube and kept under an argon atmosphere. Lithium in small pieces (4 mg, 0.58 mmol) was added and the mixture sonicated for 1.75 h keeping the temperature of the bath at 6–8 °C. After 5 min the solution took a green color that remained all the time. Then, the above solution cooled to 0 °C was added to a cold (ice-bath) solution of imide **9** (100 mg, 0.23 mmol) in anhydrous THF (0.5 mL) and the brown solution was reacted at this temperature for 1 h and at room temperature for 12 h. Water (4 mL) was added and the mixture was extracted with $CH_2Cl_2$ (4×4 mL). The combined organic phases were dried (anhydrous $Na_2SO_4$) and concentrated to dryness in vacuo to give a solid residue (166 mg), which analyzed by GC–MS showed to be mainly 4,4′-di-*t*-butylbiphenyl and reduction products derived from it. The aqueous phase was made acidic with 2 N HCl and extracted with AcOEt (3×4 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a solid residue, consisting mainly of **10** (56 mg).

### 5.12. 1,8-Diphenyl-*N*-methyl-15-oxahexacyclo-[6.6.1.1$^{2,5}$.1$^{4,7}$.0$^{2,7}$.0$^{9,14}$]heptadeca-9,11,13-triene-4,5-dicarboximide (19)

To a cold (−78 °C) solution of diiodide **9** (100 mg, 0.23 mmol) and 1,3-diphenylisobenzofuran (DPIBF, 73 mg, 0.27 mmol) in anhydrous THF (3 mL), a solution of *t*-BuLi (0.7 M in *n*-pentane, 0.3 mL, 0.21 mmol) was added dropwise. After 30 min at −78 °C, the mixture was allowed to heat to room temperature, methanol (1 mL) and water (5 mL) were added and it was extracted with diethyl ether (3×10 mL). The combined organic extracts were dried (anhydrous $Na_2SO_4$) and concentrated in vacuo to give a yellowish solid (162 mg), which was submitted to column chromatography [neutral aluminum oxide (16 g), column diameter: 1.5 cm, heptane/AcOEt mixtures]. On elution with a mixture heptane/AcOEt in the ratio of 97:3, slightly impure compound **19** (83 mg) was isolated. An analytical sample of **19** (30 mg, 29% yield) was obtained as a white crystalline solid, mp 246–247 °C, by crystallization of the above product from isopropanol (3 mL). IR (KBr): $\nu$ 3033, 2997, 2939, 1764, 1700 (C=O st), 1601, 1497, 1473, 1448, 1426, 1370, 1347, 1318, 1261, 1129, 1009, 981, 753, 700, 684 cm$^{-1}$. $^1$H NMR: $\delta$ 1.62 [dd, $J$=8.7 Hz, $J'$=3.5 Hz, 2H, 3(16)-H$_\alpha$], 1.95 [dm, $J$=8.7 Hz, 2H, 6(17)-H$_\beta$], 2.09 [dm, $J$=8.7 Hz, 2H, 3(16)-H$_\beta$], 2.18 [dd, $J$=8.7 Hz, $J'$=3.5 Hz, 2H, 6(17)-H$_\alpha$], 2.92 (s, 3H, N-CH$_3$), 7.03 [m, 2H, 10(13)-H], 7.16 [m, 2H, 11(12)-H], 7.39 (tm, $J$=7.5 Hz, 2H, ArH$_{para}$), 7.47 (m, 4H, ArH$_{meta}$), 7.59 (dm, $J$=8.0 Hz, 4H, ArH$_{ortho}$). $^{13}$C NMR (100.6 MHz): $\delta$ 24.6 (CH$_3$, N-*C*H$_3$), 49.3 [CH$_2$, C3(16)], 49.4 [CH$_2$, C6(17)], 57.8 (C, C4), 58.1 (C, C5), 70.1 [C, C2(7)], 87.3 [C, C1(8)], 120.3 [CH, C10(13)], 125.5 (CH, ArC$_{ortho}$), 127.3 [CH, C11(12)], 127.9 (CH, ArC$_{para}$), 128.6 (CH, ArC$_{meta}$), 136.7 (C, ArC$_{ipso}$), 146.8 [C, C9(14)], 174.5 [C, 4*C*ON)], 174.8 [C, 5*C*ON)]. MS (EI), *m/z* (%): 460 (13), 459 (M$^{\bullet+}$, 35), 355 (29), 354 (92), 270 [(C$_{20}$H$_{14}$O)$^{\bullet+}$, 48], 269 (23), 253 (20), 252 (31), 241 (32), 239 (43), 226 (31), 217 (24), 215 (25), 202 (30), 189 [(M−C$_{20}$H$_{14}$O)$^{\bullet+}$, 26], 165 (46), 105

($C_6H_5CO^+$, 100), 77 (51). Elemental analysis: calcd for $C_{31}H_{25}NO_3 \cdot 0.25H_2O$ (464.05): C 80.24, H 5.54, N 3.02. Found: C 80.24, H 5.65, N 2.77.

### 5.13. Reaction of imide 9 with 0.45% sodium amalgam

Imide **9** (100 mg, 0.23 mmol) and 1,4-dioxane (2.2 mL) were added to 0.45% sodium amalgam, previously prepared from sodium (63 mg, 2.9 mmol) and mercury (13.9 g), and the mixture was vigorously stirred for 3.5 h under an argon atmosphere. The mixture was filtered through a pad of Celite® under reduced pressure washing the solid with diethyl ether ($3\times10$ mL) and $CH_2Cl_2$ (5 mL). The combined filtrate and washings were concentrated to dryness in vacuo to give a solid residue (37 mg), which by GC–MS showed the presence of three main components (14, 55, and 9% relative areas), whose MS spectra suggest them to be **21**, **20**, and starting **9**. MS spectrum of **21**: (EI), m/z (%): 191 ($M^{\bullet+}$, 8), 134 [(M−CONMe)$^{\bullet+}$, 26], 106 [(M−CONMeCO)$^{\bullet+}$, 100], 105 (18), 93(19), 92(28), 91(39), 78(25), 65(21). MS spectrum of **20**: (EI), m/z (%): 317 ($M^+$, 20), 232 [(M−CONMeCO)$^{\bullet+}$, 31], 190 [(M−I)$^+$, 34], 133 (23), 105 [(M−CONMeCO−I)$^+$, 100], 93 (21).

## Acknowledgements

Financial support from *Ministerio de Ciencia y Tecnología* (Project CTQ2005-02192) and *Comissionat per a Universitats i Recerca* (Project 2005-SGR-00180) is gratefully acknowledged. We thank the *Centre de Supercomputació de Catalunya* (CESCA) for computational facilities, the *Serveis Científico-Tècnics* of the University of Barcelona for the NMR and MS facilities, and Ms. P. Domènech from the II-QAB (CSIC, Barcelona, Spain) for carrying out the elemental analyses.

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