

# Attempted synthesis of 2-oxo-*N*-phenyltetracyclo[7.2.1.0<sup>2,6</sup>.0<sup>5,11</sup>]-dodecane-9,10-dicarboximide by intramolecular $\alpha$ -ketocarbene insertion into an unactivated C-H bond

Pelayo Camps,<sup>a\*</sup> José A. Fernández,<sup>a</sup> Santiago Vázquez,<sup>a</sup>  
Mercè Font-Bardia,<sup>b,c</sup> and Xavier Solans<sup>b</sup>

<sup>a</sup>Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, Av. Diagonal 643, E-08028, Barcelona, Spain

<sup>b</sup>Departament de Cristal·lografia, Mineralogia i Dipòsits Minerals. Facultat de Geologia, Universitat de Barcelona, Av. Martí Franquès, s/n, E-08028 Barcelona, Spain

<sup>c</sup>Unitat de Difracció de RX, Centre Científic i Tecnològic de la Universitat de Barcelona (CCiTUB), Universitat de Barcelona, Solé i Sabarís 1-3. 08028 Barcelona

E-mail: [camps@ub.edu](mailto:camps@ub.edu)

Dedicated to Prof. Rita Hoyos de Rossi (65<sup>th</sup> anniversary)  
and Prof. Julio Cesar Podestá (70<sup>th</sup> anniversary)

DOI: <http://dx.doi.org/10.3998/ark.5550190.0012.729>

---

## Abstract

The diastereoselective preparation of 4 $\alpha$ -(diazomethylcarbonyl)-*N*-phenyltricyclo[5.2.1.0<sup>2,6</sup>]-decane-2 $\beta$ ,6 $\beta$ -dicarboximide and attempts to transform this compound into a derivative containing the tetracyclo[7.2.1.0<sup>2,6</sup>.0<sup>5,11</sup>]dodecane skeleton are described.

**Keywords:** 9-Borabicyclo[3.3.1]nonane, diastereoselective hydroboration,  $\alpha$ -diazoketone, attempted intramolecular  $\alpha$ -ketocarbene C-H insertion

---

## Introduction

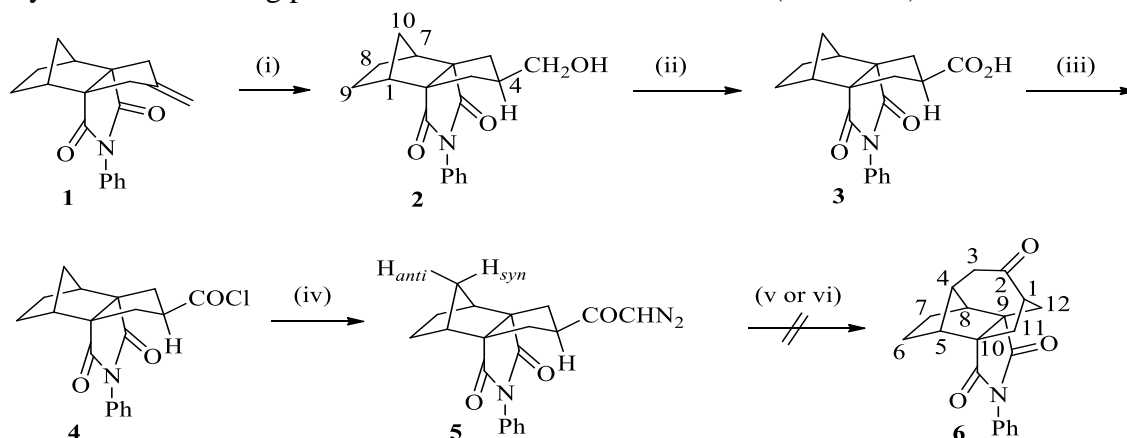
We have been working for many years on the preparation and reactivity of different cage compounds.<sup>1</sup> We have recently prepared different amine derivatives containing several of these skeletons to study their biological activity with quite interesting results.<sup>2</sup>

With the aim of preparing novel cage compounds as scaffolds for the preparation of new derivatives with potential biological activity, we planned the preparation of compound **6** containing the tetracyclo[7.2.1.0<sup>2,6</sup>.0<sup>5,11</sup>]dodecane skeleton (Scheme 1). Only one paper describing two compounds containing this carbocyclic skeleton prepared from a longifolene derivative have so far been described.<sup>3</sup> However, the methods used for the preparation of these compounds

can not be generally applied to obtain compounds with this carbocyclic skeleton. Recently, we described an easy access to compound **1** (Scheme 1) by double alkylation of the dianion derived from *endo*-*N*-phenylnorbornane-2,3-dicarboximide with 3-chloro-2-chloromethyl-1-propene.<sup>4</sup> We envisaged that compound **6** might be prepared from alkene **1** as shown in Scheme 1, the key-step consisting of an intramolecular insertion of an  $\alpha$ -ketocarbene, generated from diazoketone **5**, into an unactivated C-H bond with formation of a seven-membered ring. These types of transformations are well known and have been widely applied to the elaboration of three to six-membered rings, formation of five-membered rings being usually preferred.<sup>5</sup> The formation of seven-membered rings by intramolecular  $\alpha$ -ketocarbene insertions into S-H, O-H or N-H bonds is well known.<sup>5b</sup> Several examples of carbene insertions into an unactivated C-H bond leading to seven-membered heterocycles (oxepanes,<sup>6</sup> or 1,2-oxazepines<sup>6a</sup>) or even larger heterocycles<sup>7</sup> have been described. Intramolecular C-H insertion of the  $\alpha$ -ketocarbene derived from diazoketone **5** can not lead to a five-membered ring, although it might give a three- or four-membered ring. Insertion at the bridgehead positions leading to a six-membered ring must be very unfavorable for steric reasons. Consequently, it appeared to us that there was a real chance for the  $\alpha$ -ketocarbene derived from **5** to insert into the C-H<sub>syn</sub> bond of the methylene bridge leading to the tetracyclo[7.2.1.0<sup>2,6</sup>.0<sup>5,11</sup>]dodecane skeleton with formation of a seven-membered ring competing with the other possible intramolecular C-H insertions.

## Results and Discussion

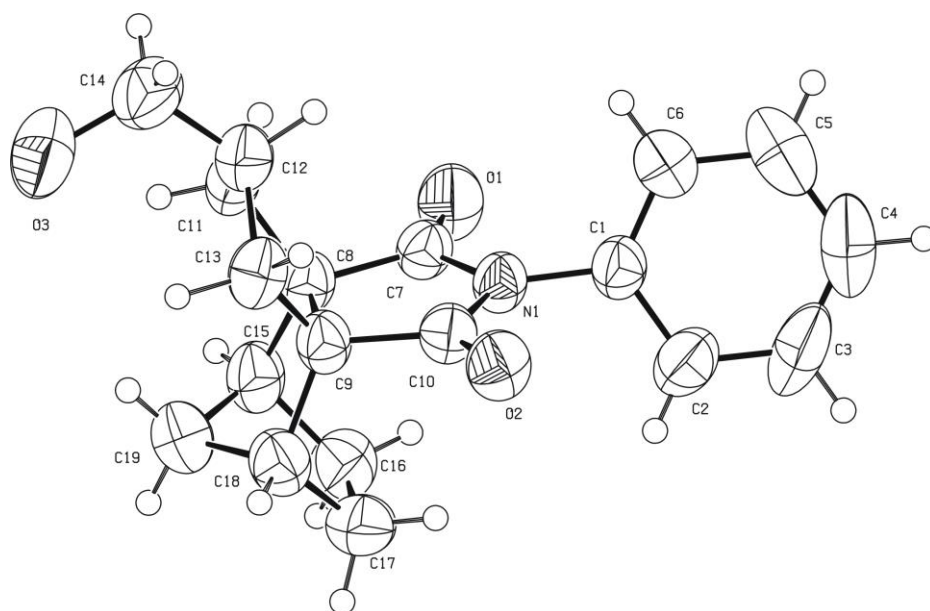
Hydroboration of alkene **1** with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by oxidation of the formed borane with H<sub>2</sub>O<sub>2</sub> under standard conditions<sup>8</sup> gave, after column chromatography, alcohol **2** in 76% yield. Worthy of note, only the desired stereoisomer was obtained, in accord with hydroboration taking place at the less hindered alkene face (Scheme 1).



**Scheme 1.** Synthetic approach to tetracycle **6**. (i) (a) 9-BBN, THF, 0 °C, 4 h; (b) 30% H<sub>2</sub>O<sub>2</sub>, 3N NaOH, rt, 15 min, **2** (76%); (ii) CrO<sub>3</sub>, 5M H<sub>2</sub>SO<sub>4</sub>, acetone, 0→25 °C, 1 h, **3** (77%); (iii) SOCl<sub>2</sub>,

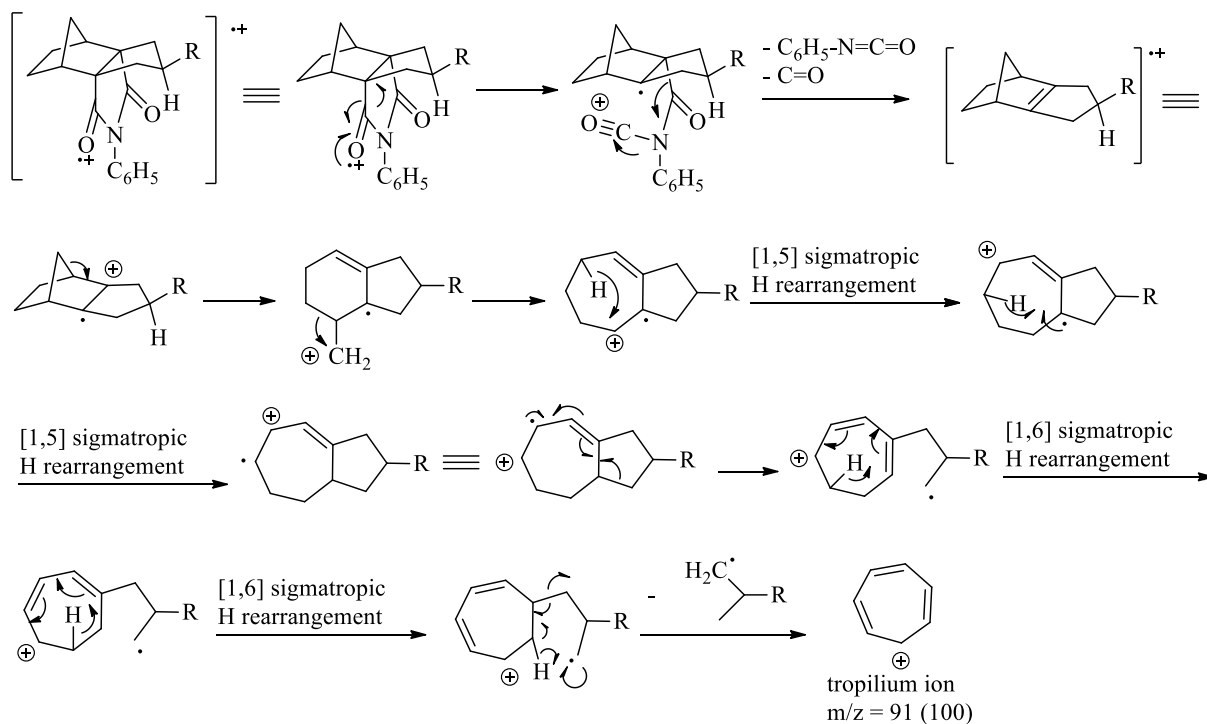
reflux, 4 h; (iv) excess  $\text{CH}_2\text{N}_2$  in  $\text{Et}_2\text{O}$ , **5** (58% from **3**); (v) *n*-Pentane, quartz reactor, hv, 5 h; (vi)  $[\text{Rh}(\text{pfb})_2]_2$  (about 10% mol),  $\text{CH}_2\text{Cl}_2$ , rt, 30 min.

The configuration of alcohol **2** could not be unambiguously determined by  $^1\text{H}$  and  $^{13}\text{C}$  NMR in spite of the absence of NOE between 4-H and 10- $\text{H}_{\text{syn}}$ , however, it was clearly established by X-ray diffraction analysis (Figure 1). Oxidation of alcohol **2** with Jones reagent<sup>9</sup> gave the corresponding carboxylic acid **3** in good yield. Reaction of acid **3** with thionyl chloride followed by reaction with an excess of an ethereal solution of diazomethane, prepared as described,<sup>10</sup> gave diazoketone **5** in 58% yield, after column chromatography. Photochemical decomposition of diazoketone **5** in *n*-pentane solution using a quartz reactor and a 125 W low pressure mercury lamp gave a mixture of compounds, none of them having the expected molecular mass (GC/MS) for the tetracyclic ketone **6**. A similar result was obtained when diazoketone **5** was decomposed at room temperature in  $\text{CH}_2\text{Cl}_2$  in the presence of the complex dirhodium tetra(perfluorobutyrate)( $[\text{Rh}(\text{pfb})_2]_2$ ).



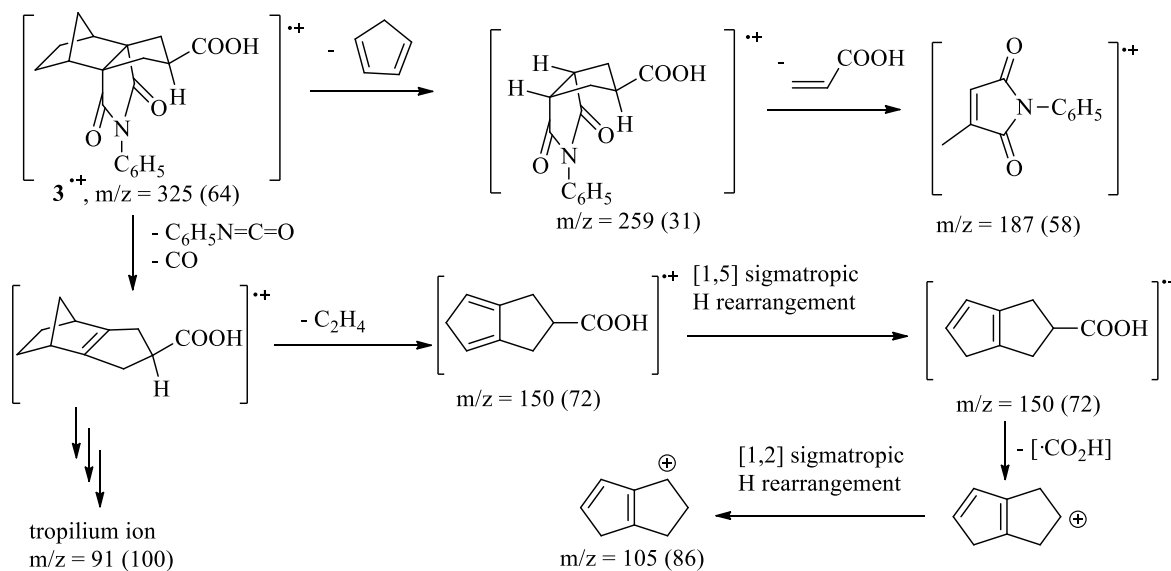
**Figure 1.** X-Ray diffraction structure (ORTEP) of alcohol **2**.

The new compounds **2**, **3** and **5** were fully characterized through their spectroscopic data (IR, MS,  $^1\text{H}$  and  $^{13}\text{C}$  NMR) and elemental analysis. Worthy of note, the MS spectra (electron impact, 70 eV) of compounds **3** and **5** showed a base peak with  $m/z = 91$  Da, an ion which was also abundant in the MS spectrum of compound **2**. Although this ion could correspond to  $[\text{C}_6\text{H}_5\text{N}]^+$ , it might also correspond to the tropilium ion  $[\text{C}_7\text{H}_7]^+$ . This assumption was supported by the fact that many sandalwood odorants containing the same tricyclo[5.2.1.0<sup>2,6</sup>]decane skeleton and lacking any aniline group also show abundant peaks of  $m/z = 91$  Da, which in one case was the base peak.<sup>11</sup> A possible pathway for the formation of the tropilium ion by fragmentation of the parent ion of compounds **2**, **3** or **5** is given in Scheme 2.

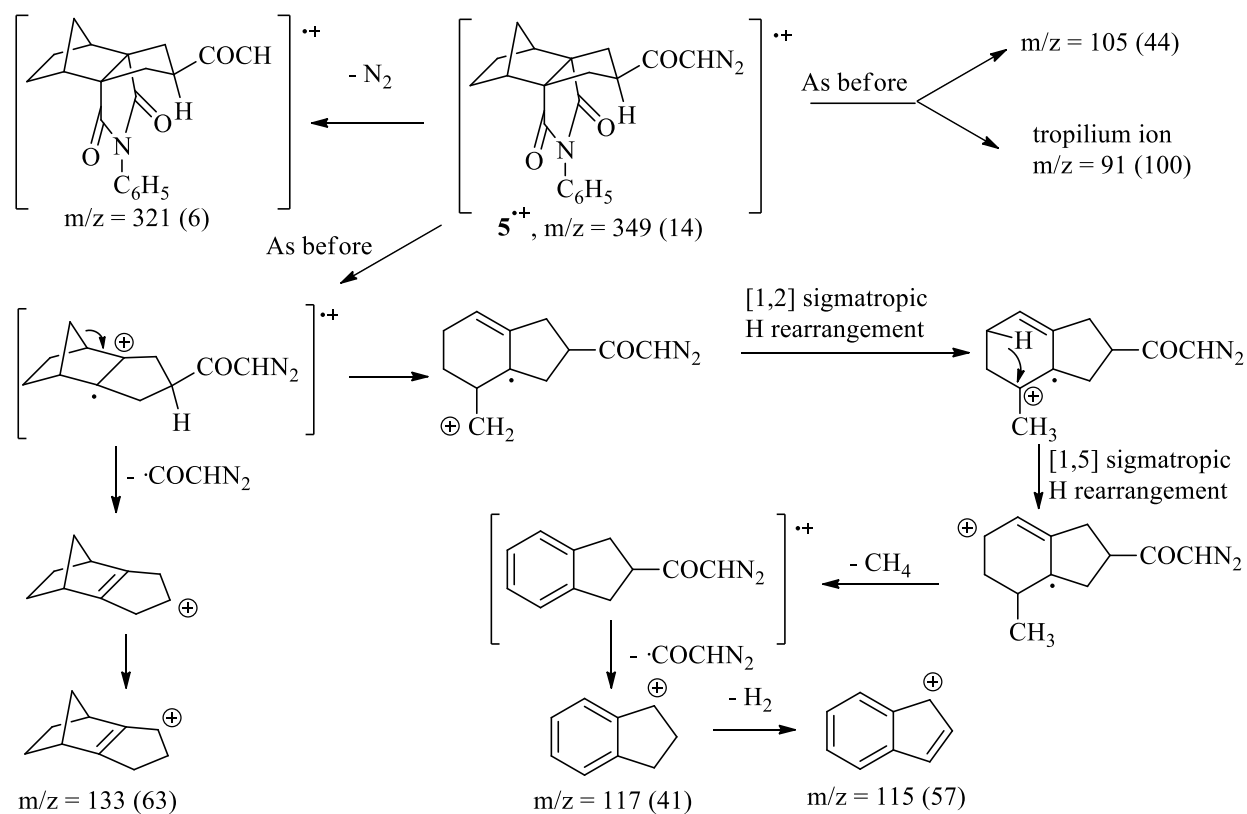


**Scheme 2.** Possible pathway for the formation of tropilium ion in the MS spectra of compounds **2**, **3** and **5**.

A tentative structure for the main ions observed in the MS spectra of acid **3** and diazoketone **5** as well as possible mechanistic pathways for the formation of most of them is given in Schemes 3 and 4, respectively. Fragmentation of alcohol **2** essentially parallels that of acid **3**, although in this case the parent peak is the base peak.



**Scheme 3.** Possible structures and pathways for the formation of the main ions in the MS spectrum of compound **3**.



**Scheme 4.** Possible structures and pathways for the formation of the main ions in the MS spectrum of compound **5**.

## Conclusions

$\alpha$ -Diazoketone **5** has been prepared in a diastereoselective way from compound **1**. However, attempts to transform **5** into ketone **6**, containing the tetracyclo[7.2.1.0<sup>2,6</sup>.0<sup>5,11</sup>]dodecane skeleton, by photochemical or Rh-catalyzed intramolecular  $\alpha$ -ketocarbene insertion into the unactivated C(10)-H<sub>syn</sub> bond with formation of a seven-membered carbocycle, were fruitless.

## Experimental Section

**General.** Melting points were determined with a MFB 595010 M Gallenkamp melting point apparatus.  $^1H$  NMR spectra were recorded on Varian Gemini-300 (300 MHz) or Varian VXR-500 (500 MHz) spectrometers.  $^{13}C$  NMR spectra were recorded on a Varian Gemini-300 (75.4 MHz) spectrometer. The  $^1H/^1H$  homocorrelation spectra (COSY and NOESY) and the one bond and long range  $^1H/^{13}C$  heterocorrelation spectra (gHSQC and gHMBC, respectively) were performed on a Varian VXR-500 spectrometer. Chemical shifts are given in  $\delta$  scale and the

coupling constants in Hz. IR spectra were registered on a FTIR Perkin–Elmer Spectrum RX1 spectrometer, only the more intense absorption bands are given. MS and GC/MS were carried out on a Hewlett-Packard HP-5988A spectrometer, the sample being introduced directly or through a gas chromatograph (Hewlett-Packard model 5890 Series II) using a 30-m column (HP-45, 5% diphenyl-95% dimethylpolysiloxane), conditions: 10 psi, initial temperature 100 °C (2 min), then heating at a rate of 10 °C/min till 250 °C, then isothermic. The electron impact technique (EI, 70 eV) was used. Only significant ions are given: those with higher relative ratio, except for the ions with higher  $m/z$  values. The elemental analyses were determined in a Carlo Erba model 1106 equipment at the IIQAB (CSIC) of Barcelona, Spain. For the column chromatography, silica gel 60 AC (35–70  $\mu\text{M}$ , SDS, ref. 2000027) was used. Thin-layer chromatography (TLC) was performed on aluminum-backed sheets with silica gel 60 F<sub>254</sub> (Merck, ref. 1.05554) and spots were visualized with UV light, a 1% aqueous solution of  $\text{KMnO}_4$  or by placing the sheets in an iodine atmosphere.

**4 $\alpha$ -(Hydroxymethyl)-*N*-phenyltricyclo[5.2.1.0<sup>2,6</sup>]decane-2 $\beta$ ,6 $\beta$ -dicarboximide (2).** To a cold (0 °C, ice-water bath) and magnetically stirred solution of alkene **1** (1.87 g, 6.37 mmol) in anhydrous THF (80 mL) under an argon atmosphere, a solution of 9-borabicyclo[3.3.1]nonane (9-BBN, 37 mL, 0.5 M in THF, 18.5 mmol) was added dropwise and the mixture was stirred at 0 °C for 4 h. After addition of EtOH (6.7 mL), the mixture was allowed to warm to room temperature and aqueous solutions of 30%  $\text{H}_2\text{O}_2$  (6.7 mL) and 3 M NaOH (8.3 mL) were simultaneously added dropwise in 5 min, occasionally cooling with a water bath and the reaction mixture was stirred at room temperature for 15 min. Water (40 mL) was added and the mixture was extracted with EtOAc (3  $\times$  80 mL). The combined organic extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to dryness *in vacuo* to give a residue (4.89 g) that was subjected to column chromatography (silica gel, 152 g, hexane/EtOAc). On elution with hexane/EtOAc 1:1, alcohol **2** (1.50 g, 76%) was obtained as colorless crystals, mp 152.7–153.5 °C (from  $\text{Et}_2\text{O}$ ); IR (KBr):  $\nu$  3490s, 2960m, 2947m, 2882w, 2835w, 1772w and 1697s (C=O st), 1494w, 1385s, 1290w, 1191w, 1174m, 1150m, 1083w, 734m  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.35–1.40 [m, 3H, 8(9)- $\text{H}_\beta$  and OH], 1.45–1.50 [m, 2H, 3(5)- $\text{H}_\alpha$ ], 1.49–1.57 (m, 1H, 10- $\text{H}_{anti}$ ), 1.64–1.69 [m, 2H, 8(9)- $\text{H}_\alpha$ ], 1.84–1.89 (dm,  $J = 10.5$  Hz, 1H, 10- $\text{H}_{syn}$ ), 2.03 (tquint,  $J = 12.0$  Hz,  $J' = 6.0$  Hz, 1H, 4- $\text{H}_\beta$ ), 2.46 [dd,  $J = 13.5$  Hz,  $J' = 6.0$  Hz, 2H, 3(5)- $\text{H}_\beta$ ], 2.57–2.60 [m, 2H, 1(7)-H], 3.65 (d,  $J = 6.0$  Hz, 2H, 3- $\text{CH}_2\text{OH}$ ), 7.10–7.24 (m, 2H, Ar- $\text{H}_{ortho}$ ), 7.36–7.40 (tm,  $J = 7.0$  Hz, 1H, Ar- $\text{H}_{para}$ ), 7.44–7.48 (m, 2H, Ar- $\text{H}_{meta}$ );  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.8 [ $\text{CH}_2$ , C8(9)], 37.7 [ $\text{CH}_2$ , C3(5) and C10], 41.4 (CH, C4), 43.3 [CH, C1(7)], 63.9 ( $\text{CH}_2\text{OH}$ ), 64.3 [C, C2(6)], 126.5 (CH, Ar- $\text{C}_{ortho}$ ), 128.6 (CH, Ar- $\text{C}_{para}$ ), 129.1 (CH, Ar- $\text{C}_{meta}$ ), 131.9 (C, Ar- $\text{C}_{ipso}$ ), 180.2 (CON); GC/MS (retention time 26.4 min),  $m/z$  (%): 312 (25), 311 ( $\text{M}^+$ , 100), 245 (65), 187 (47), 136 (31), 117 (21), 105 (26), 91 (26); Anal. calcd. for  $\text{C}_{19}\text{H}_{21}\text{NO}_3$ : C, 73.3; H, 6.8; N, 4.5. Found: C, 72.9; H, 6.8; N, 4.4%.

**4 $\alpha$ -(Hydroxycarbonyl)-*N*-phenyltricyclo[5.2.1.0<sup>2,6</sup>]decane-2 $\beta$ ,6 $\beta$ -dicarboximide (3).** A solution of Jones reagent was prepared by adding  $\text{CrO}_3$  (1.13 g, 11.3 mmol) to aqueous 5 M

H<sub>2</sub>SO<sub>4</sub> (4.5 mL) and stirring till complete dissolution. To a cold (0 °C, ice-water bath) solution of alcohol **2** (618 mg, 2.0 mmol) in acetone (15 mL), part of the Jones reagent prepared above (3.0 mL, 6.8 mmol H<sub>2</sub>CrO<sub>4</sub>) was added dropwise keeping the temperature at 0 °C. Then, the reaction mixture was stirred at 0 °C to room temperature for 1 h. Diethyl ether (20 mL) and water (15 mL) were added and the mixture was extracted with aqueous 2 M NaOH (3 × 20 mL). The combined aqueous extracts were acidified till pH 1 with aqueous 10% HCl and were extracted with Et<sub>2</sub>O (4 × 30 mL). The combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to dryness *in vacuo* to give a residue (598 mg) that was subjected to column chromatography (silica gel, 15 g, EtOAc), yielding acid **3** as colorless crystals (500 mg, 77%), mp 232.3–233.5 °C (from Et<sub>2</sub>O); IR (KBr):  $\nu$  3300–2800 [max. at 3050w, 2967m, 2885w], 1774w, 1708s (C=O st), 1599w, 1503w, 1458w, 1432w, 1378m, 1318w, 1297w, 1272w, 1232m, 1186w, 1171w, 1145m, 910w, 889w, 729m, 689w cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.34–1.46 [m, 2H, 8(9)-H $\beta$ ], 1.55 (d,  $J$  = 11.1 Hz, 1H, 10-H $_{anti}$ ), 1.65–1.78 [m, 2H, 8(9)-H $\alpha$ ], 1.89–2.00 [m, 3H, 10-H $_{syn}$  and 3(5)-H $\alpha$ ], 2.65–2.74 [m, 5H, 1(7)-H, 3(5)-H $\beta$  and 4-H $\beta$ ], 7.19–7.28 (m, 2H, Ar-H $_{ortho}$ ), 7.37–7.44 (m, 1H, Ar-H $_{para}$ ), 7.44–7.52 (m, 2H, Ar-H $_{meta}$ ), 10.4–11.6 (br s, 1H, CO<sub>2</sub>H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  24.7 [CH<sub>2</sub>, C8(9)], 37.7 (CH<sub>2</sub>, C10), 38.3 [CH<sub>2</sub>, C3(5)], 42.7 (CH, C4), 43.4 [CH, C1(7)], 63.7 [C, C2(6)], 126.5 (CH, Ar-C $_{ortho}$ ), 128.8 (CH, Ar-C $_{para}$ ), 129.2 (CH, Ar-C $_{meta}$ ), 131.7 (C, Ar-C $_{ipso}$ ), 178.9 (CO<sub>2</sub>H), 179.3 (CON). MS,  $m/z$  (%): 325 (M<sup>+</sup>, 64), 259 (31), 187 (58), 150 (72), 105 (86), 104 (48), 91 (100), 77 (79), 67 (59), 65 (66). Anal. calcd. for C<sub>19</sub>H<sub>19</sub>NO<sub>4</sub>: C, 70.1; H, 5.9; N, 4.3. Found: C, 69.9; H, 5.9; N, 4.2%.

**4 $\alpha$ -(Diazomethylcarbonyl)-N-phenyltricyclo[5.2.1.0<sup>2,6</sup>]decane-2 $\beta$ ,6 $\beta$ -dicarboximide (5).** A stirred solution of acid **3** (566 mg, 1.7 mmol) in SOCl<sub>2</sub> (6.7 mL) was heated under reflux for 4 h. The solution was allowed to cool to room temperature and was concentrated *in vacuo*. The residue was taken in anhydrous toluene (20 mL) and concentrated to dryness *in vacuo* and this process was repeated once again. The residue consisting of the corresponding acid chloride **4** (585 mg, 98%) was used as such in the next step. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.34–1.50 [m, 2H, 8(9)-H $\beta$ ], 1.59 (d,  $J$  = 11.4 Hz, 1H, 10-H $_{anti}$ ), 1.64–1.80 [m, 2H, 8(9)-H $\alpha$ ], 1.90 (d,  $J$  = 11.4 Hz, 1H, 10-H $_{syn}$ ), 2.02 [t,  $J$  = 13.2 Hz, 2H, 3(5)-H $\alpha$ ], 2.67 [s, 2H, 1(7)-H], 2.82 [dd,  $J$  = 13.2 Hz,  $J'$  = 7.2 Hz, 2H, 3(5)-H $\beta$ ], 3.00–3.20 (m, 1H, 4-H $\beta$ ), 7.20–7.28 (m, 2H, Ar-H $_{ortho}$ ), 7.40–7.51 (m, 3H, Ar-H $_{para}$  and Ar-H $_{meta}$ ); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>):  $\delta$  24.6 [CH<sub>2</sub>, C8(9)], 37.7 (CH<sub>2</sub>, C10), 38.2 [CH<sub>2</sub>, C3(5)], 43.5 [CH, C1(7)], 54.1 (CH, C4), 63.2 [C, C2(6)], 126.4 (CH, Ar-C $_{ortho}$ ), 128.8 (CH, Ar-C $_{para}$ ), 129.3 (CH, Ar-C $_{meta}$ ), 131.6 (C, Ar-C $_{ipso}$ ), 173.9 (COCl), 178.6 (CON).

To a cold (0 °C, ice-water bath) and magnetically stirred solution of acid chloride **4** (562 mg, 1.65 mmol) in anhydrous Et<sub>2</sub>O (50 mL), an excess of an ethereal solution of diazomethane (15 mL, about 10 mmol) was added.<sup>8</sup> The mixture was stirred at 0 °C for 30 min and was allowed to warm to room temperature for 16 h. The solution was concentrated to dryness *in vacuo* to give a residue (767 mg) that was subjected to column chromatography (silica gel, 21 g, hexane/EtOAc). On elution with hexane/EtOAc 8:2, diazoketone **5** (335 mg, 58%) was obtained as yellow crystals, mp 152.7–154.2 °C (from Et<sub>2</sub>O). IR (KBr):  $\nu$  3088m, 2962m, 2883w, 2112s (C=N<sup>+</sup>=N<sup>-</sup>)

st), 1775w, 1705s (C=O st), 1619s, 1495m, 1373s, 1314m, 1303m, 1173s, 1147s, 732m  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.35–1.40 [m, 2H, 8(9)- $\text{H}_\beta$ ], 1.53 (d,  $J = 10.8$  Hz, 1H, 10- $\text{H}_{anti}$ ), 1.64–1.73 [m, 2H, 8(9)- $\text{H}_\alpha$ ], 1.93–2.01 [m, 3H, 10- $\text{H}_{syn}$  and 3(5)- $\text{H}_\alpha$ ], 2.51–2.64 [m, 5H, 1(7)-H, 3(5)- $\text{H}_\beta$  and 4- $\text{H}_\beta$ ], 5.27 (s, 1H, CH- $\text{N}_2$ ), 7.20–7.30 (m, 2H, Ar- $\text{H}_{ortho}$ ), 7.39–7.41 (m, 1H, Ar- $\text{H}_{para}$ ), 7.41–7.56 (m, 2H, Ar- $\text{H}_{meta}$ );  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.7 [ $\text{CH}_2$ , C8(9)], 37.7 [ $\text{CH}_2$ , C10], 38.2 [C3(5)], 43.5 [CH, C1(7)], 48.2 (CH, C4), 55.0 (CH- $\text{N}_2$ ), 63.7 [C, C2(6)], 126.4 (CH, Ar- $\text{C}_{ortho}$ ), 128.7 (CH, Ar- $\text{C}_{para}$ ), 129.2 (CH, Ar- $\text{C}_{meta}$ ), 131.8 (C, Ar- $\text{C}_{ipso}$ ), 179.5 (CON), 193.3 (C4-CO); MS,  $m/z$  (%): 349 ( $\text{M}^+$ , 14), 321 ( $[\text{M}-\text{N}_2]^+$ , 6), 254 (8), 224 (7), 174 (12), 146 (19), 133 (63), 117 (41), 115 (57), 105 (44), 104 (44), 92 (39), 91 (100), 79 (46), 78 (45), 77 (94), 67 (88), 65 (62); Anal. calcd. for  $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_3$ : C, 68.8; H, 5.5; N, 12.0. Found: C, 69.0; H, 5.7; N, 11.3%.

**Photochemical decomposition of diazoketone (5).** A solution of diazoketone **5** (52 mg, 0.15 mmol) in anhydrous *n*-pentane (30 mL) was placed in a quartz reactor with magnetic stirring and argon atmosphere and it was irradiated with a medium pressure 125 W mercury lamp for 5 h. The solution was concentrated *in vacuo* and the residue was analyzed by  $^1\text{H}$  and  $^{13}\text{C}$  NMR showing the presence of compounds structurally related to the starting compound. GC/MS analysis of the above residue showed the presence of 4 main products: retention time (min) (%  $\text{M}^+$ ): 22.8 (12.9, 279), 23.2 (46.9, 281), 24.6 (12.5, 295), 25.9 (20.8, 339). None of them showed the expected molecular mass for ketone **6**.

**Thermal decomposition of diazoketone (5) in the presence of  $[\text{Rh}(\text{pfb})_2]_2$ .** To a magnetically stirred solution of  $[\text{Rh}(\text{pfb})_2]_2$  (2.8 mg, 2.5  $\mu\text{mol}$ ) in anhydrous  $\text{CH}_2\text{Cl}_2$  (5 mL), a solution of diazoketone **5** (79 mg, 0.23 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (1 mL) was slowly added (9 h). The solution was stirred for 30 min, was filtered through a pad of silica gel (2 g), washing the solid with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 50$  mL). The combined filtrate and washings were concentrated *in vacuo* and the residue was analyzed by  $^1\text{H}$  and  $^{13}\text{C}$  NMR without detecting the formation of the expected ketone **6**. GC/MS analysis of the crude product showed the presence of three main products: retention time (min) (%  $\text{M}^+$ ): 25.9 (16.4, 339), 26.2 (17.7, 339), 27.3 (65.9, 367). None of them showed the expected molecular mass for ketone **6**.

**X-Ray crystallography of alcohol (2).** A prismatic crystal (0.1  $\times$  0.1  $\times$  0.2 mm) was selected and mounted on a MAR345 diffractometer with an image plate detector. Unit-cell parameters were determined from 97 reflections ( $3 < \theta < 31^\circ$ ) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo  $\text{K}\alpha$  radiation. 31138 reflections were measured in the range  $3.46 \leq \theta \leq 31.30$ . 5452 of which were non-equivalent by symmetry [ $R_{int}(\text{on } I) = 0.032$ ]. 3518 reflections were assumed as observed applying the condition  $I > 2\sigma(I)$ . Lorentz-polarization and absorption corrections were made. The structure was solved by Direct methods, using SHELXS computer program<sup>12</sup> and refined by full-matrix least-squares method with SHELX97 computer program,<sup>13</sup> using 31138 reflections (very negative intensities were not assumed). The function minimized was  $\sum w | |F_o|^2 - |F_c|^2 |^2$ , where  $w = [\sigma^2(I) + (0.0706P)^2]^{-1}$ , and  $P = (|F_o|^2 - 2|F_c|^2)/3$ ,  $f$ ,  $f'$  and  $f''$  were taken from International Tables of X-Ray Crystallography.<sup>14</sup> 5 H atoms were located from a difference synthesis and refined with



an overall isotropic temperature factor and 16H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom to which are linked. The final R(on F) factor was 0.048,  $wR(\text{on } |F|^2) = 0.1189$  and goodness of fit = 0.999 for all observed reflections. Number of refined parameters was 228. Max. shift/esd = 0.00, mean shift/esd = 0.00. Max. and min. peaks in final difference synthesis was 0.234 and  $-0.316 \text{ e}\text{\AA}^{-3}$ , respectively.

CCDC 762131 contains the supplementary crystallographic data of this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), or by emailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk), or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

**Table 1.** Crystal data and structure refinement of compound **2**

Molecular formula	C <sub>19</sub> H <sub>21</sub> NO <sub>3</sub>
Molecular mass	311.37
Crystal system	Orthorhombic
Space group	Pbca
Cell parameters	
<i>a</i> (Å)	13.631 (4)
<i>b</i> (Å)	23.301 (10)
<i>c</i> (Å)	11.137 (6)
<i>V</i> (Å <sup>3</sup> )	3537 (3)
<i>Z</i>	8
<i>F</i> (000)	1328
<i>d</i> <sub>calcd.</sub> [Mg m <sup>-3</sup> ]	1.169
Crystal size (mm)	0.2×0.1×0.1
Measured reflect.	31138
Independent reflect.	5452
Observed reflect.	3518
μ(Mo Kα) (mm <sup>-1</sup> ) <sup>a</sup>	0.079
<i>R</i>	0.048
<i>R</i> <sub>w</sub>	0.1189
Δρ <sub>max</sub> <sup>b</sup> (e Å <sup>-3</sup> )	0.234
Δρ <sub>min</sub> <sup>c</sup> (e Å <sup>-3</sup> )	-0.316
Refined parameters	229
Max. shift/esd	0.00

<sup>a</sup>μ(Mo Kα) linear absorption coefficient. Radiation Mo Kα (λ = 0.71073 Å).

<sup>b</sup>Maximum peaks in final difference synthesis.

<sup>c</sup>Minimum peaks in final difference synthesis.

## Acknowledgements

Financial support from Ministerio de Ciencia e Innovación (CTQ2008-03768) and Comissionat per a Universitats i Recerca (2005-SGR-00180) is gratefully acknowledged.

## References

1. (a) Vázquez, S.; Camps, P. *Tetrahedron* **2005**, *61*, 5147 and references therein cited. (b) Ayats, C.; Camps, P.; Font-Bardia, M.; Muñoz, M. R.; Solans, X.; Vázquez, S. *Tetrahedron* **2006**, *62*, 7436. (c) Camps, P.; Muñoz, M. R.; Vázquez, S. *Tetrahedron* **2006**, *62*, 7645. (d) Ayats, C.; Camps, P.; Fernández, J. A.; Vázquez, S. *Chem. Eur. J.* **2007**, *13*, 1522. (e) Camps, P.; Colet, G.; Delgado, S.; Muñoz, M. R.; Pericàs, M. A.; Solà, L.; Vázquez, S. *Tetrahedron* **2007**, *63*, 4669. (f) Ayats, C.; Camps, P.; Font-Bardia, M.; Solans, X.; Vázquez, S. *Tetrahedron* **2007**, *63*, 8027. (g) Camps, P.; Fernández, J. A.; Vázquez, S. *Arkivoc* **2010**, *IV*, 74.
2. (a) Camps, P.; Duque, M. D.; Vázquez, S.; Naesens, L.; De Clerq, E.; Sureda, F. X.; López-Querol, M.; Camins, A.; Pallàs, M.; Prathalingam, S. R.; Kelly, J. M.; Romero, V.; Ivorra, D.; Cortés, D. *Bioorg. Med. Chem.* **2008**, *16*, 9925. (b) Duque, M. D.; Camps, P.; Profire, L.; Montaner, S.; Vázquez, S.; Sureda, F. X.; Mallol, J.; López-Querol, M.; Naesens, L.; De Clerq, E.; Prathalingam, S. R.; Kelly, J. M. *Bioorg. Med. Chem.* **2009**, *17*, 3198. (c) Duque, M. D.; Camps, P.; Torres, E.; Valverde, E.; Sureda, F. X.; López-Querol, M.; Camins, A.; Prathalingam, S. R.; Kelly, J. M.; Vázquez, S. *Bioorg. Med. Chem.* **2010**, *18*, 46. (d) Torres, E.; Duque, M. D.; Camps, P.; Naesens, L.; Calvet, T.; Font-Bardia, M.; Vázquez, S. *ChemMedChem* **2010**, *5*, 2072.
3. Jadhav, P. K.; Nayak, U. R. *Indian J. Chem.* **1978**, *16B*, 1047.
4. Camps, P.; Fernández, J. A.; Rull, J.; Vázquez, S. *Eur. J. Org. Chem.* **2009**, 3081.
5. (a) Slattery, C. N.; Ford, A.; Maguire, A. R. *Tetrahedron* **2010**, *66*, 6681. (b) Ye, T.; McKerverey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (c) Padwa, A.; Krumpe, K. *Tetrahedron* **1992**, *48*, 5385. (d) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765. (e) Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75. (f) Burke, S. D.; Grieco, P. A. *Org. React.* **1979**, *26*, 361.
6. (a) Wang, J.; Stefane, B.; Jaber, D.; Smith, J. A. I.; Vickery, C.; Diop, M.; Sitim, H. O. *Angew. Chem. Int. Ed.* **2010**, *49*, 3964. (b) Lee, E.; Choi, I.; Song, S. Y. *J. Chem. Soc., Chem. Commun.* **1995**, 321.
7. Doyle, M. P.; Protopopova, M. N. *J. Am. Chem. Soc.* **1995**, *117*, 7281.
8. Komiotis, D.; Lim, C. T.; Dieter, J. P.; Le Breton, G. C.; Venton, D. L. *J. Med. Chem.* **1992**, *35*, 3033.
9. Ruedi, G.; Nagel, M.; Hansen, H.-J. *Org. Lett.* **2003**, *5*, 2691.
10. (a) Arndt, F. *Org. Synth. Coll. Vol. II*, **1943**, 165. (b) Arndt, F. *Org. Synth. Coll. Vol. II*, **1943**, 461.

11. Buchbauer, G.; Stappen, I.; Pretterklieber, C.; Wolschann, P. *Eur. J. Med. Chem.* **2004**, *39*, 1039.
12. Sheldrick, G. M. *SHELXS: A Computer Program for Automatic Solution of Crystal Structure Refinement*; University of Göttingen: Germany, 1997.
13. Sheldrick, G. M. *SHELX-97: A Computer Program for Crystal Structure Refinement*; University of Göttingen: Germany, 1999.
14. *International Tables of X-ray Crystallography*; Knoch Press: Birmingham, 1974; Vol IV, pp 99–100 and 149.