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V.A. Tartakovskii on his 75th Anniversary

## Product Structure in the Reaction of Dimethyl Acetylenedicarboxylate with 2-Furyl-1,2,3,4-tetrahydroquinolines

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**Abstract**—Dimethyl acetylenedicarboxylate reacts with 4-substituted and 3,4-fused 2-furyl-1,2,3,4-tetrahydroquinoline derivatives at the furan fragment according to the [4+2]-cycloaddition pattern. The reaction is not stereoselective, and it yields two diastereoisomeric 7-oxabicyclo[2.2.1]hepta-2,5-dienes whose structure was determined by X-ray analysis and NMR spectroscopy.

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We recently showed [1, 2] that [4+2]-cycloaddition of maleic anhydride and acryloyl chloride to 2-furyl-substituted tetrahydrofuro(pyrano)[3,2-*c*]quinolines **A** obtained by the Povarov reaction [3, 4] gives mixtures of isomeric epoxyisoindolotetrahydroquinolinones **B** differing by mutual arrangement of the epoxy bridge and substituents in the tetrahydropyridine fragment (Scheme 1). The reaction involves acylation of the nitrogen atom, followed by intramolecular cycloaddition of the activated C=C bond to the furan ring [5, 6].

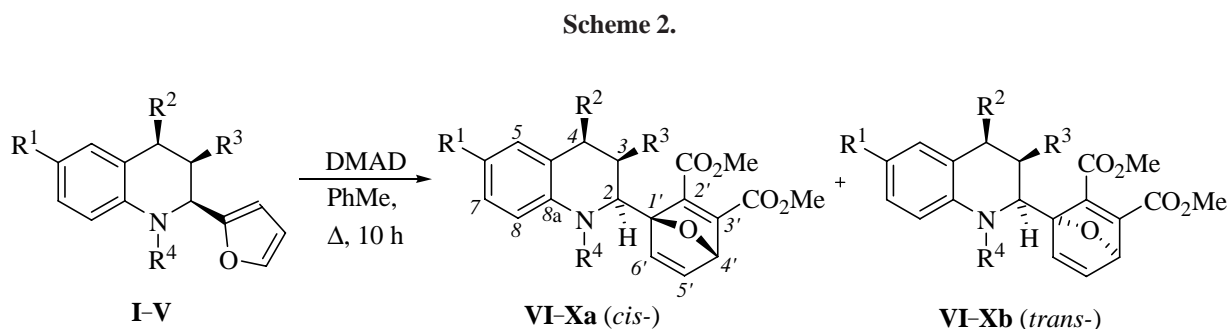
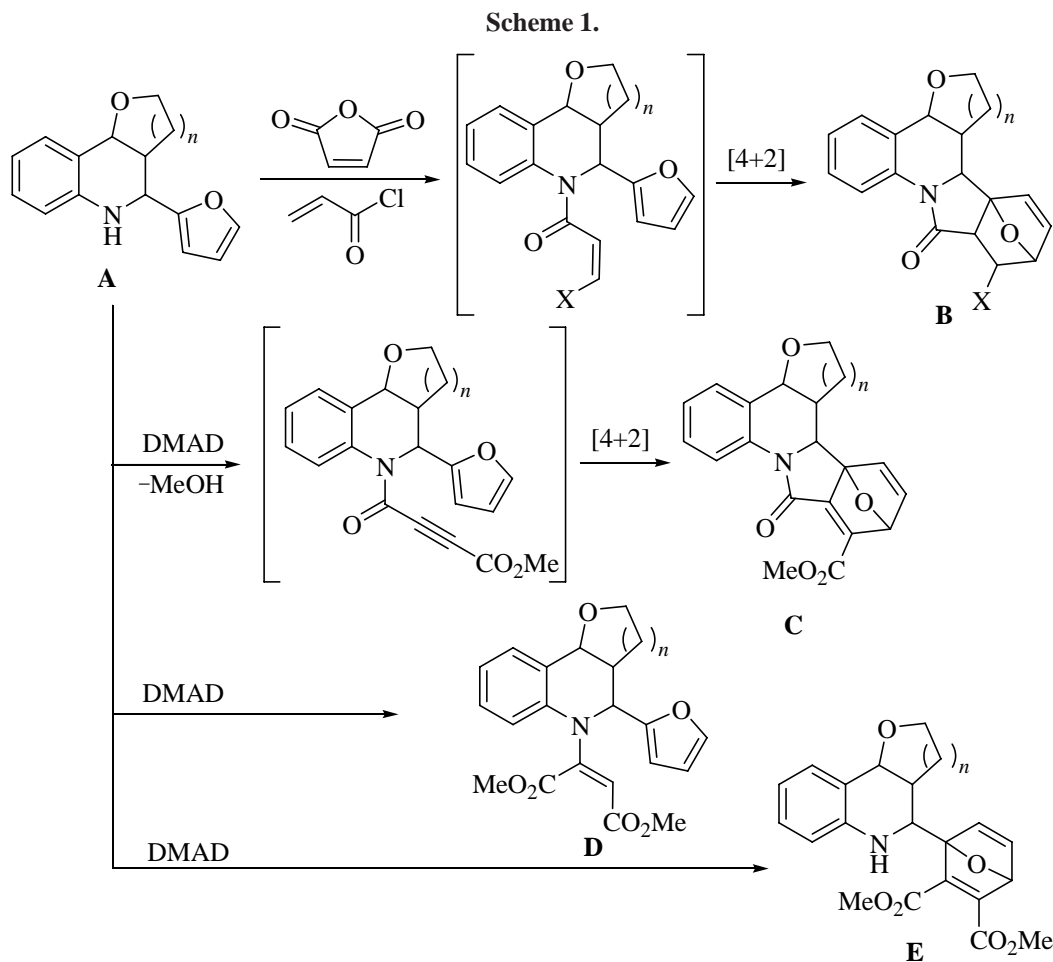
It seemed to be interesting to examine reactions of 2-furyl-substituted tetrahydroquinolines **A** with dimethyl acetylenedicarboxylate (DMAD) as active dienophile and electrophile. Furyl-substituted quinolines possess two centers capable of reacting with DMAD: nucleophilic nitrogen atom and furan ring which constitutes an electron-rich diene fragment. Attack on DMAD molecule by the nitrogen atom may occur in two directions. The first of these is aminolysis of the ester group in DMAD and subsequent intramolecular cycloaddition, leading to fused polycyclic epoxyisoindoles like **C**. The second path involves Michael-type addition of the nitrogen atom at the triple bond of DMAD to form N-vinyl-substituted 2-furyltetrahydroquinolines **D**. Finally, cycloaddition of DMAD at the furan ring could give Diels–Alder adducts **E** which may be formed as mixtures of stereoisomers

due to restricted rotation of the furan ring about the C<sup>2</sup>–C<sup>22</sup> bond (Scheme 1).

Our results showed that *cis*-2-furyltetrahydrofuro(pyrano)quinolines **I–V** react with DMAD in boiling toluene only at the furan ring to give the corresponding isomeric Diels–Alder adducts **VI–X** in 32–88% yield (Scheme 2). No reaction occurred at room temperature. Alternative addition products that could be formed via addition at the quinoline nitrogen atom (compounds **C** and **D**) were not detected.

Restricted rotation of the furan ring in molecules **I–V** gives rise to the possibility for DMAD molecule to approach the furan ring from two sides; as a result, diastereoisomeric *cis* and *trans* adducts **VI–X** are formed (Scheme 3). According to the <sup>1</sup>H NMR data, the ratio of isomers **a** and **b** is 1 : 2 for adducts **VI** and **VII**, 1 : 3 for **IX**, and 1 : 1 for **VIII** and **X**, and it does not change on prolonged heating of the reaction mixture in the presence of excess DMAD. This means that the cycloaddition is irreversible.

All ten isomers **VIa–Xa** and **VIb–Xb** were isolated as individual substances by fractional crystallization, and we were able to examine their steric structure. In the <sup>1</sup>H NMR spectra of cycloaddition products **VI–X** we observed a characteristic set of signals from the H<sup>4'</sup>–H<sup>6'</sup> protons ( $J_{4',5'} \approx 2.0$ ,  $J_{5',6'} \approx 5.3$  Hz) in the oxabicyclohepta-



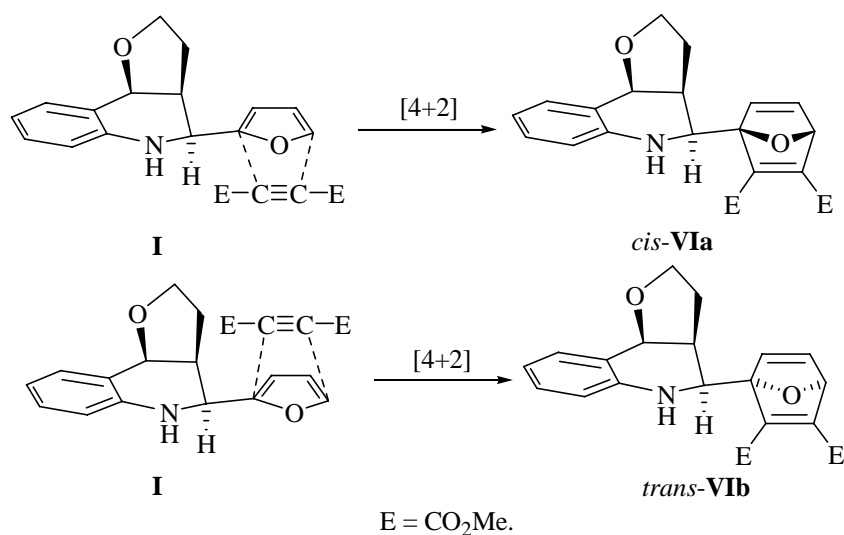
**I, VI:**  $R^1, R^4 = H, R^2, R^3 = O(CH_2)_2$ ; **II, VII:**  $R^1 = Me, R^2, R^3 = O(CH_2)_2, R^4 = H$ ; **III, VIII:**  $R^1 = H, R^2, R^3 = O(CH_2)_2, R^4 = Ac$ ; **IV, IX:**  $R^1, R^4 = H, R^2, R^3 = O(CH_2)_3$ ; **V, X:**  $R^1, R^3, R^4 = H, R^2 = 2$ -pyrrolidin-1-yl.

diene fragment [7]. In the  $^{13}C$  NMR spectra, the most informative were downfield signals from  $C^1$  ( $\delta_C$  98–100 ppm),  $C^{2',3'}$  ( $\delta_C$  149–153 ppm),  $C^4$  ( $\delta_C$  ~83.5 ppm), and  $C^{5',6'}$  ( $\delta_C$  142–145 ppm). However, it is obvious that the NMR data do not ensure unambiguous assignment of individual isomers **VI–X** to the *cis* or *trans* series **a** or

**b**. Therefore, the structure of compound **VIa** was studied by X-ray analysis of its single crystal.

According to the X-ray diffraction data (see figure), the tetrahydropyridine fragment in **VIa** adopts a *twist* conformation with the  $C^{11}$  and  $C^{12}$  atoms deviating by 0.181 and  $-0.498$  Å, respectively, from the plane formed

## Scheme 3.



by the four remaining atoms C<sup>15</sup>C<sup>16</sup>C<sup>21</sup>N<sup>1</sup>. The tetrahydrofuran and oxabicyclo[2.2.1]heptadiene fragments have their usual conformations.

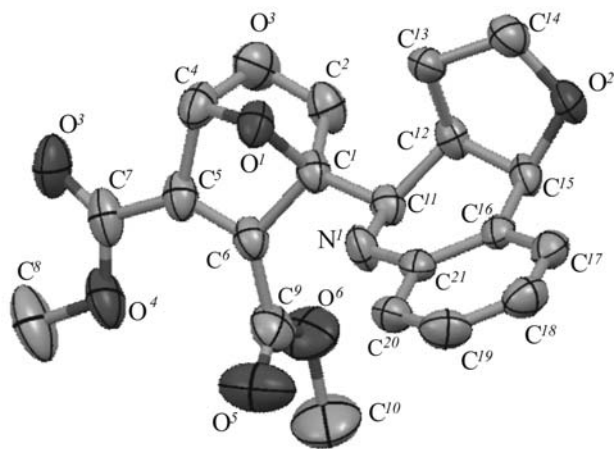
Comparison of the NMR spectra of diastereoisomers **VIa** and **VIb** with known configurations allowed us to find out some specific features that may be useful for the assignment of the other isomers of **VI–IX** to the **a** or **b** series. In particular, diastereoisomers **a** and **b** are characterized by appreciably different chemical shifts of H<sup>5'</sup> and H<sup>6'</sup>. The H<sup>6'</sup> signal in the spectra of **VIa–IXa** is a doublet at  $\delta$  7.19–7.24, and the H<sup>5'</sup> signal appears as a doublet of doublets at  $\delta$  7.31–7.37 ppm. In the <sup>1</sup>H NMR spectra of **VIb–IXb**, the H<sup>5'</sup> and H<sup>6'</sup> signals are arranged in the reversed order, at  $\delta$  7.29–7.31 and 7.15–7.17 ppm, respectively. In the <sup>13</sup>C NMR spectra, the difference in

the chemical shifts of the olefinic carbon atoms C<sup>2'</sup> and C<sup>3'</sup> in the oxabicycloheptadiene fragment ( $\delta_C$  151–156 ppm) may be used as a criterion for the assignment of stereoisomers. The  $\Delta\delta$  value for isomers **VIa–IXa** is 3.9–5.6, whereas it is as small as 0.4–1.2 ppm for isomers **VIb–IXb**. No such difference is observed for *N*-acylated adducts **X**.

Thus the results of the present study showed that the reaction of dimethyl acetylenedicarboxylate with 2-furylquinolines follows only the [4+2]-cycloaddition pattern with participation of the furan ring. Stereochemical structure of the diastereoisomeric Diels–Alder adducts were established, and NMR signals characteristic of particular diastereoisomers were found.

## EXPERIMENTAL

Commercial reagents from Acros Organics were used without additional purification. The IR spectra were recorded in KBr on an Infracum FT-801 spectrometer with Fourier transform. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured at 30°C on a Bruker Advance-600 spectrometer at 600.13 and 150 MHz, respectively, from solutions in CDCl<sub>3</sub> using the solvent signals as reference (CHCl<sub>3</sub>,  $\delta$  7.26 ppm; CDCl<sub>3</sub>,  $\delta_C$  77.0 ppm). Signals in the <sup>13</sup>C NMR spectra were assigned using DEPT and JMODECHO pulse sequences, as well as HMQC and COSY-45 two-dimensional correlation techniques. The mass spectra (electron impact, 70 eV) were run on a Finnigan MAT-95-XL mass spectrometer with direct sample admission into the ion source. Thin-layer



Structure of the molecule of dimethyl 1-(2,3,3a,4,5,9b-xahydrofuro[3,2-c]quinolin-4-yl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (**VIa**).

chromatography was performed on Sorbfil plates (development with iodine vapor). Neutral aluminum oxide (Brockmann activity grade 0) or Al<sub>2</sub>O<sub>3</sub> Fluka-507S (grain size 0.05–0.15 mm) was used for column chromatography.

X-Ray analysis of a single crystal of compound **VIa** was performed on an Enraf–Nonius CAD-4 four-circle diffractometer at 293 K ( $\lambda$ MoK $\alpha$  irradiation, graphite monochromator,  $\omega$ -scanning,  $\theta/2\theta = 60^\circ$ ,  $\lambda = 0.71073 \text{ \AA}$ ). The structure was solved by the direct method using SHELXS-97 program [8] and was refined by the least-squares procedure in anisotropic approximation using SHELXL-97 program [9]. Crystal size 0.33×0.15×0.12 mm, light yellow prisms, C<sub>21</sub>H<sub>21</sub>NO<sub>6</sub>, *M* 383.39; space group *P*-1, triclinic crystal system; unit cell parameters: *a* = 8.909(2), *b* = 9.339(2), *c* = 13.783(3) Å;  $\alpha = 71.32(3)$ ,  $\beta = 89.65(3)$ ,  $\gamma = 63.05(3)^\circ$ ; *V* = 955.2(4) Å<sup>3</sup>; *Z* = 2; *d*<sub>calc</sub> = 1.333 g/cm<sup>3</sup>;  $\mu = 0.098 \text{ mm}^{-1}$ . Total of 3516 reflections were measured, 3362 of which were independent [*R*<sub>int</sub> = 0.0172, *F*(000) = 404]. The complete set of crystallographic parameters was deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 617483).

**1-[4-(2-Furyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinolin-5-yl]ethanone (III).** A solution of 5.00 g (21 mmol) of tetrahydroquinoline **I** in 40 ml of acetic anhydride was heated for 2 h under reflux. The mixture was cooled, poured into 50 ml of water, and neutralized with 25% aqueous ammonia, and the precipitate was filtered off and recrystallized from hexane–ethyl acetate. Yield 3.25 g (76%), colorless crystals, mp 144–146°C, *R*<sub>f</sub> 0.53 (hexane–ethyl acetate, 1 : 1). IR spectrum:  $\nu$  1635 cm<sup>-1</sup> (C=O). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 283 (6) [*M*]<sup>+</sup>, 254 (6), 238 (55), 212 (12), 196 (100), 167 (10), 146 (12), 130 (10), 115 (10), 91 (11), 77 (10), 43 (14), 28 (26). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.61 m (1H, 9-H), 7.28 m (2H, 7-H, 8-H), 7.18 d.d (1H, 52 -H, *J*<sub>52,32</sub> = 0.7, *J*<sub>52,42</sub> = 1.8 Hz), 7.13 br.s (1H, 6-H), 6.36 br.s (1H, 4-H), 6.07 d.d (1H, 42 -H, *J*<sub>52,42</sub> = 1.8, *J*<sub>42,32</sub> = 3.2 Hz), 5.55 d (1H, 32 -H, *J*<sub>52,32</sub> = 0.8, *J*<sub>32,42</sub> = 3.2 Hz), 4.75 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 7.9 Hz), 3.75 q (1H, 2-H<sub>A</sub>, *J*<sub>2A,2B</sub> = 8.3, *J*<sub>2A,3A</sub> = 8.0, *J*<sub>2A,3B</sub> = 8.0 Hz), 3.68 d.t (1H, 2-H<sub>B</sub>, *J*<sub>2A,2B</sub> = 8.3, *J*<sub>2B,3B</sub> = 8.0, *J*<sub>2B,3A</sub> = 4.6 Hz), 3.15 m (1H, 3a-H, *J*<sub>3a,9b</sub> = 7.9 Hz), 2.26 s (3H, COMe), 2.17 m (1H, 3-H<sub>A</sub>), 1.76 m (1H, 3-H<sub>B</sub>). Found, %: C 72.4; H 6.2; N 4.5. C<sub>17</sub>H<sub>17</sub>NO<sub>3</sub>. Calculated, %: C 72.1; H 6.0; N 4.9. *M* 283.12.

**General procedure for the synthesis of Diels–Alder adducts VI–X.** Dimethyl acetylenedicarboxylate,

0.75 ml (6.0 mmol), was added to a solution of 4.0 mmol of tetrahydroquinoline **I–V** in 20 ml of toluene, and the mixture was heated for 10 h under reflux. The solvent was removed under reduced pressure, and the residue (yellowish crystals) was recrystallized from hexane–ethyl acetate. Individual stereoisomeric adducts **VIa–Xa** and **VIb–Xb** were isolated by fractional recrystallization from hexane–ethyl acetate.

**Dimethyl 1-(2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinolin-4-yl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (VIa/VIb).** Overall yield 67%. Addukt **VIa**: orange crystals, mp 156–158°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.37 (hexane–ethyl acetate, 2 : 1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3402 (NH); 1737, 1707 (C=O). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 383 (12) [*M*]<sup>+</sup>, 240 (63), 196 (88), 174 (42), 130 (100), 117 (65), 77 (50), 39 (52). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.31 d (1H, 9-H, *J*<sub>8,9</sub> = 7.6 Hz), 7.31 d.d (1H, 52 -H, *J*<sub>4',5'</sub> = 2.1, *J*<sub>5',6'</sub> = 5.2 Hz), 7.15 d (1H, 62 -H, *J*<sub>5',6'</sub> = 5.2 Hz), 7.07 t (1H, 7-H, *J*<sub>6,7</sub> = 7.6 Hz), 6.81 t (1H, 8-H, *J*<sub>8,9</sub> = 7.6 Hz), 6.59 d (1H, 6-H, *J*<sub>6,7</sub> = 7.6 Hz), 5.75 d (1H, 42 -H, *J*<sub>4',5'</sub> = 2.1 Hz), 5.27 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 7.6 Hz), 4.40 d (1H, 4-H, *J*<sub>3a,4</sub> = 1.9 Hz), 3.86 s and 3.81 s (3H each, CO<sub>2</sub>Me), 3.80 m (2H, 2-H), 2.13 m (1H, 3-H<sub>A</sub>), 1.91 m (1H, 3-H<sub>B</sub>), 2.76 m (1H, 3a-H). <sup>13</sup>C NMR spectrum,  $\delta$ <sub>C</sub>, ppm: 24.9 t (C<sup>3</sup>), 39.8 d (C<sup>3a</sup>), 50.7 d (C<sup>4</sup>), 52.3 q and 52.7 q (CO<sub>2</sub>Me), 67.1 t (C<sup>2</sup>), 76.0 d (C<sup>9b</sup>), 83.3 d (C<sup>4</sup>), 99.2 s (C<sup>1</sup>), 115.5 d (C<sup>6</sup>), 119.4 d (C<sup>8</sup>), 122.7 s (C<sup>9a</sup>), 128.2 d (C<sup>7</sup>), 129.6 d (C<sup>9</sup>), 142.2 d (C<sup>6'</sup>), 143.7 s (C<sup>5a</sup>), 145.2 d (C<sup>5</sup>), 151.6 s and 155.5 s (C<sup>2'</sup>, C<sup>3</sup>), 162.2 s and 165.4 s (CO<sub>2</sub>Me). Found, %: C 66.11; H 5.60; N 3.50. C<sub>21</sub>H<sub>21</sub>NO<sub>6</sub>. Calculated, %: C 65.79; H 5.52; N 3.65. *M* 383.14.

Addukt **VIb**: light yellow crystals, mp 174–176°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.43 (hexane–ethyl acetate, 2 : 1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3319 (NH), 1713 (C=O). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 383 (40) [*M*]<sup>+</sup>, 240 (100), 196 (90), 174 (50), 130 (60), 77 (25), 39 (21). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.35 d (1H, 62 -H, *J*<sub>5',6'</sub> = 5.2 Hz), 7.34 d.d (1H, 9-H, *J*<sub>8,9</sub> = 7.5, *J*<sub>7,9</sub> = 1.1 Hz), 7.24 d.d (1H, 52 -H, *J*<sub>4',5'</sub> = 1.9, *J*<sub>5',6'</sub> = 5.2 Hz), 7.10 d.t (1H, 7-H, *J*<sub>7,9</sub> = 1.1, *J*<sub>7,8</sub> = 7.5 Hz), 6.82 t (1H, 8-H, *J*<sub>7,8</sub> = 7.5 Hz), 6.64 d (1H, 6-H, *J*<sub>6,7</sub> = 7.5 Hz), 5.77 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.9 Hz), 5.21 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 7.7 Hz), 4.35 d (1H, 4-H, *J*<sub>3a,4</sub> = 2.1 Hz), 3.87 s and 3.84 s (3H each, CO<sub>2</sub>Me), 3.81 m (2H, 2-H), 2.11 m (1H, 3-H<sub>A</sub>), 1.89 m (1H, 3-H<sub>B</sub>), 2.74 m (1H, 3a-H). <sup>13</sup>C NMR spectrum,  $\delta$ <sub>C</sub>, ppm: 24.9 t (C<sup>3</sup>), 39.9 d (C<sup>3a</sup>), 51.5 d (C<sup>4</sup>), 52.4 q and 52.7 q (CO<sub>2</sub>Me), 67.1 t (C<sup>2</sup>), 75.9 d (C<sup>9b</sup>),

84.0 d (C<sup>4</sup>), 98.2 s (C<sup>1</sup>), 115.4 d (C<sup>6</sup>), 128.6 d (C<sup>8</sup>), 122.8 s (C<sup>9a</sup>), 129.0 d (C<sup>7</sup>), 130.0 d (C<sup>9</sup>), 143.5 d (C<sup>5</sup>), 141.6 s (C<sup>5a</sup>), 143.9 d (C<sup>6</sup>), 153.5 s and 154.5 s (C<sup>2</sup>, C<sup>3</sup>), 162.6 s and 165.5 s (CO<sub>2</sub>Me). Found, %: C 66.13; H 5.65; N 3.55. C<sub>21</sub>H<sub>21</sub>NO<sub>6</sub>. Calculated, %: C 65.79; H 5.52; N 3.65. *M* 383.14.

**Dimethyl 1-(8-methyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinolin-4-yl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (VIIIa/VIIIb).** Overall yield 52%. Adduct **VIIIa**: dark yellow crystals, mp 110–112°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.63 (hexane–ethyl acetate, 2:1). IR spectrum, ν, cm<sup>-1</sup>: 3394 (NH), 1726 (C=O). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 397 (33) [*M*]<sup>+</sup>, 255 (100), 210 (78), 188 (24), 144 (63), 111 (21), 91 (20), 59 (18). <sup>1</sup>H NMR spectrum, δ, ppm: 7.30 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 2.0, *J*<sub>5',6'</sub> = 5.3 Hz), 7.15 d (1H, 9-H, *J*<sub>7,9</sub> = 2.1 Hz), 7.15 d (1H, 62 -H, *J*<sub>5',6'</sub> = 5.3 Hz), 6.90 d.d (1H, 7-H, *J*<sub>7,9</sub> = 2.1, *J*<sub>6,7</sub> = 8.1 Hz), 6.54 d (1H, 6-H, *J*<sub>6,7</sub> = 8.1 Hz), 5.76 d (1H, 4'-H, *J*<sub>4',5'</sub> = 2.0 Hz), 5.25 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 7.8 Hz), 4.34 d (1H, 4-H, *J*<sub>3a,4</sub> = 1.8 Hz), 3.85 s and 3.82 s (3H each, CO<sub>2</sub>Me), 3.83 m (2H, 2-H), 2.13 m (1H, 3-H<sub>A</sub>), 1.88 m (1H, 3-H<sub>B</sub>), 2.76 m (1H, 3a-H). <sup>13</sup>C NMR spectrum, δ<sub>C</sub>, ppm: 20.5 q (8-Me), 25.0 t (C<sup>3</sup>), 39.8 d (C<sup>3a</sup>), 50.9 d (C<sup>4</sup>), 52.3 q and 52.7 q (CO<sub>2</sub>Me), 67.1 t (C<sup>3</sup>), 76.1 d (C<sup>9b</sup>), 83.3 d (C<sup>4</sup>), 99.3 s (C<sup>1</sup>), 115.8 d (C<sup>6</sup>), 128.8 d (C<sup>8</sup>), 122.8 s (C<sup>9a</sup>), 129.0 d (C<sup>7</sup>), 129.7 d (C<sup>9</sup>), 141.4 s (C<sup>5a</sup>), 142.2 d (C<sup>6</sup>), 145.2 d (C<sup>5</sup>), 151.4 s and 155.6 s (C<sup>2</sup>, C<sup>3</sup>), 162.3 s and 165.4 s (CO<sub>2</sub>Me). Found, %: C 66.43; H 5.67; N 3.58. C<sub>22</sub>H<sub>23</sub>NO<sub>6</sub>. Calculated, %: C 66.49; H 5.83; N 3.52. *M* 397.43.

Adduct **VIIIb**: yellow crystals, mp 160–162°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.68 (hexane–ethyl acetate, 2:1). IR spectrum, ν, cm<sup>-1</sup>: 3354 (NH); 1730, 1702 (C=O). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 397 (81) [*M*]<sup>+</sup>, 255 (100), 210 (88), 188 (32), 144 (74), 111 (30), 91 (35), 77 (33), 59 (66), 39 (90). <sup>1</sup>H NMR spectrum, δ, ppm: 7.36 d (1H, 6'-H, *J*<sub>5',6'</sub> = 5.3 Hz), 7.24 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.8, *J*<sub>5',6'</sub> = 5.3 Hz), 7.15 d (1H, 9-H, *J*<sub>7,9</sub> = 1.6 Hz), 6.92 d.d (1H, 7-H, *J*<sub>7,9</sub> = 1.6, *J*<sub>6,7</sub> = 8.0 Hz), 6.57 d (1H, 6-H, *J*<sub>6,7</sub> = 8.0 Hz), 5.76 d (1H, 42 -H, *J*<sub>4',5'</sub> = 1.8 Hz), 5.18 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 7.8 Hz), 4.30 d (1H, 4-H, *J*<sub>3a,4</sub> = 2.1 Hz), 3.87 s and 3.84 s (3H each, CO<sub>2</sub>Me), 3.80 m (2H, 2-H), 2.12 m (1H, 3-H<sub>A</sub>), 1.89 m (1H, 3-H<sub>B</sub>), 2.74 m (1H, 3a-H). <sup>13</sup>C NMR spectrum, δ<sub>C</sub>, ppm: 20.4 q (8-Me), 24.8 t (C<sup>3</sup>), 39.7 d (C<sup>3a</sup>), 51.3 d (C<sup>4</sup>), 52.4 q and 52.7 q (CO<sub>2</sub>Me), 67.0 t (C<sup>2</sup>), 75.7 d (C<sup>9b</sup>), 84.0 d (C<sup>4</sup>), 98.1 s (C<sup>1</sup>), 115.2 d (C<sup>6</sup>), 119.3 d (C<sup>8</sup>),

122.8 s (C<sup>9a</sup>), 128.2 d (C<sup>7</sup>), 129.8 d (C<sup>9</sup>), 143.4 d (C<sup>5</sup>), 143.9 s (C<sup>5a</sup>), 144.0 d (C<sup>6</sup>), 153.7 s and 154.1 s (C<sup>2</sup>, C<sup>3</sup>), 162.6 s and 165.4 s (CO<sub>2</sub>Me). Found, %: C 66.45; H 5.61; N 3.54. C<sub>22</sub>H<sub>23</sub>NO<sub>6</sub>. Calculated, %: C 66.49; H 5.83; N 3.52. *M* 397.43.

**Dimethyl 1-(5-acetyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinolin-4-yl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (VIIIa/VIIIb).** Overall yield 77%. Adduct **VIIIa**: colorless crystals, mp 135–137°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.33 (hexane–ethyl acetate, 1:1). IR spectrum, ν, cm<sup>-1</sup>: 1735 (C=O, ester), 1666 (C=O, amide). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 425 (3) [*M*]<sup>+</sup>, 396 (32), 354 (33), 322 (52), 240 (31), 196 (14), 174 (16), 43 (100). <sup>1</sup>H NMR spectrum, δ, ppm: 7.50 m (1H, 9-H), 7.20–7.26 m (3H, 6-H, 7-H, 8-H), 7.02 d (1H, 6'-H, *J*<sub>5',6'</sub> = 5.2 Hz), 6.93 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.9, *J*<sub>5',6'</sub> = 5.2 Hz), 6.11 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 9.1 Hz), 5.33 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.9 Hz), 4.69 d (1H, 4-H, *J*<sub>3a,4</sub> = 9.8 Hz), 4.05 d.t (1H, 2-H<sub>A</sub>), 3.87 s and 3.69 s (3H each, CO<sub>2</sub>Me), 3.72 d.d.d (1H, 2-H<sub>B</sub>), 3.40 m (1H, 3a-H), 2.05 s (3H, COMe), 2.04 m (1H, 3-H<sub>A</sub>), 1.94 m (1H, 3-H<sub>B</sub>). <sup>13</sup>C NMR spectrum, δ<sub>C</sub>, ppm: 21.7 q (COMe), 28.1 t (C<sup>3</sup>), 42.7 d (C<sup>3a</sup>), 46.6 d (C<sup>4</sup>), 52.2 q and 52.4 q (CO<sub>2</sub>Me), 68.3 t (C<sup>2</sup>), 74.2 d (C<sup>9b</sup>), 83.8 d (C<sup>4</sup>), 100.1 s (C<sup>1</sup>), 125.8 d (C<sup>6</sup>), 126.0 d (C<sup>8</sup>), 126.8 d (C<sup>7</sup>), 127.3 d (C<sup>9</sup>), 135.1 s (C<sup>9a</sup>), 136.0 s (C<sup>5a</sup>), 142.8 d (C<sup>6</sup>), 145.2 d (C<sup>5</sup>), 149.1 s and 157.9 s (C<sup>2</sup>, C<sup>3</sup>), 162.2 s and 164.8 s (CO<sub>2</sub>Me), 169.6 s (COMe). Found, %: C 64.82; H 5.51; N 3.31. C<sub>23</sub>H<sub>23</sub>NO<sub>7</sub>. Calculated, %: C 64.93; H 5.45; N 3.29. *M* 425.44.

Adduct **VIIIb**: colorless crystals, mp 150–151°C (from hexane–ethyl acetate), *R*<sub>f</sub> 0.50 (hexane–ethyl acetate, 1:1). IR spectrum, ν, cm<sup>-1</sup>: 1712 (C=O, ester), 1651 (C=O, amide). Mass spectrum, *m/z* (*I*<sub>rel</sub>, %): 425 (5) [*M*]<sup>+</sup>, 396 (96), 383 (20), 322 (25), 296 (24), 240 (32), 196 (32), 174 (31), 130 (27), 43 (100). <sup>1</sup>H NMR spectrum, δ, ppm: 7.51 d (1H, 9-H), 7.19–7.27 m (3H, 6-H, 7-H, 8-H), 7.09 d (1H, 6'-H, *J*<sub>5',6'</sub> = 5.2 Hz), 6.98 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.8, *J*<sub>5',6'</sub> = 5.2 Hz), 6.30 d (1H, 9b-H, *J*<sub>3a,9b</sub> = 10.0 Hz), 5.33 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.8 Hz), 4.79 d (1H, 4-H, *J*<sub>3a,4</sub> = 8.5 Hz), 4.00 d.t (1H, 2-H<sub>A</sub>), 3.88 s and 3.73 s (3H each, CO<sub>2</sub>Me), 3.80 m (1H, 2-H<sub>B</sub>), 3.30 m (1H, 3a-H), 2.11 s (3H, COMe), 2.00 m (1H, 3-H<sub>A</sub>), 1.86 m (1H, 3-H<sub>B</sub>). <sup>13</sup>C NMR spectrum, δ<sub>C</sub>, ppm: 22.3 q (COMe), 27.7 t (C<sup>3</sup>), 43.6 d (C<sup>3a</sup>), 46.6 d (C<sup>4</sup>), 52.3 q and 52.6 q (CO<sub>2</sub>Me), 68.3 t (C<sup>2</sup>), 74.7 d (C<sup>9b</sup>), 83.6 d (C<sup>4</sup>), 100.0 s (C<sup>1</sup>), 125.5 d (C<sup>6</sup>), 126.0 d (C<sup>8</sup>), 126.6 d (C<sup>7</sup>), 127.2 d (C<sup>9</sup>), 135.2 s (C<sup>9a</sup>), 136.4 s (C<sup>5a</sup>), 143.2 d

(C<sup>5</sup>), 145.3 d (C<sup>6</sup>), 152.4 s and 154.4 s (C<sup>2</sup>, C<sup>3</sup>), 162.9 s and 164.1 s (CO<sub>2</sub>Me), 169.7 s (COMe). Found, %: C 64.98; H 5.47; N 3.26. C<sub>23</sub>H<sub>23</sub>NO<sub>7</sub>. Calculated, %: C 64.93; H 5.45; N 3.29. *M* 425.44.

**Dimethyl 1-(3,4,4a,5,6,10b-hexahydro-2H-pyrano-[3,2-c]quinolin-5-yl)-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (IXa/IXb).** Overall yield 52%. Adduct **IXa**: yellow crystals, mp 163–166°C (from hexane–ethyl acetate), *R<sub>f</sub>* 0.56 (hexane–ethyl acetate, 2:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3386 (NH), 1714 (C=O). Mass spectrum, *m/z* (*I<sub>rel</sub>*, %): 397 (100) [*M*]<sup>+</sup>, 338 (27), 254 (78), 196 (72), 144 (25), 130 (32), 39 (11). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.42 d.d (1H, 10-H, *J*<sub>9,10</sub> = 7.6, *J*<sub>8,10</sub> = 1.1 Hz), 7.29 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 2.0, *J*<sub>6',5'</sub> = 5.3 Hz), 7.17 d (1H, 6'-H, *J*<sub>6',5'</sub> = 5.3 Hz), 7.09 d.d.d (1H, 8-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>8,9</sub> = 7.6, *J*<sub>8,10</sub> = 1.1 Hz), 6.83 d.t (1H, 9-H, *J*<sub>9,10</sub> = *J*<sub>8,9</sub> = 7.6, *J*<sub>7,9</sub> = 1.1 Hz), 6.62 d.d (1H, 7-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>7,9</sub> = 1.1 Hz), 4.23 d (1H, 5-H, *J*<sub>4a,5</sub> = 2.1 Hz), 5.77 d (1H, 4'-H, *J*<sub>4',5'</sub> = 2.0 Hz), 5.18 d (1H, 10b-H, *J*<sub>4a,10b</sub> = 5.3 Hz), 3.82 s and 3.86 s (3H each, CO<sub>2</sub>Me), 3.41 m and 3.60 m (1H each, 2-H), 2.33 m (2H, 4a-H), 1.49 m and 2.67 m (1H each, 3-H), 1.80 m and 1.45 m (1H each, 4-H). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 19.2 t (C<sup>4</sup>), 25.0 t (C<sup>3</sup>), 33.5 d (C<sup>4a</sup>), 52.3 q and 52.4 q (CO<sub>2</sub>Me), 52.6 d (C<sup>5</sup>), 60.3 t (C<sup>2</sup>), 71.8 d (C<sup>10b</sup>), 83.5 d (C<sup>4</sup>), 99.0 s (C<sup>1</sup>), 115.4 d (C<sup>7</sup>), 118.8 d (C<sup>9</sup>), 120.5 s (C<sup>10a</sup>), 127.4 d (C<sup>10</sup>), 127.9 d (C<sup>8</sup>), 142.0 d (C<sup>6</sup>), 144.4 s (C<sup>6a</sup>), 145.0 d (C<sup>5</sup>), 150.7 s and 156.3 s (C<sup>2</sup>, C<sup>3</sup>), 162.2 s and 165.3 s (CO<sub>2</sub>Me). Found, %: C 66.7; H 5.6; N 3.5. C<sub>22</sub>H<sub>23</sub>NO<sub>6</sub>. Calculated, %: C 66.49; H 5.83; N 3.52. *M* 397.43.

Adduct **IXb**: light yellow crystals, mp 162–164°C (from hexane–ethyl acetate), *R<sub>f</sub>* 0.61 (hexane–ethyl acetate, 2:1). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3342 (NH), 1713 (C=O). Mass spectrum, *m/z* (*I<sub>rel</sub>*, %): 397 (100) [*M*]<sup>+</sup>, 338 (18), 254 (52), 196 (80), 188 (20), 144 (30), 130 (42), 77 (16), 39 (13). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.41 d.d (1H, 10-H, *J*<sub>9,10</sub> = 7.7, *J*<sub>8,10</sub> = 0.9 Hz), 7.37 d (1H, 6'-H, *J*<sub>6',5'</sub> = 5.2 Hz), 7.19 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.9, *J*<sub>6',5'</sub> = 5.2 Hz), 7.09 d.d.d (1H, 8-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>8,9</sub> = 7.7, *J*<sub>8,10</sub> = 0.9 Hz), 6.82 d.t (1H, 9-H, *J*<sub>9,10</sub> = *J*<sub>8,9</sub> = 7.7, *J*<sub>7,9</sub> = 0.9 Hz), 6.56 d.d (1H, 7-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>7,9</sub> = 0.9 Hz), 5.77 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.9 Hz), 5.12 d (1H, 10b-H, *J*<sub>4a,10b</sub> = 5.7 Hz), 4.21 d (1H, 5-H, *J*<sub>4a,5</sub> = 2.1 Hz), 3.83 s and 3.84 s (3H each, CO<sub>2</sub>Me), 3.41 m and 3.59 m (1H each, 2-H), 2.28 m (2H, 4a-H), 1.52 m and 2.67 m (1H each, 3-H), 1.80 m and 1.45 m (1H each, 4-H). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 19.0 t (C<sup>4</sup>), 25.0 t (C<sup>3</sup>), 33.4 d (C<sup>4a</sup>), 52.4 q and 52.7 q (CO<sub>2</sub>Me), 53.2 d (C<sup>5</sup>), 60.4 t (C<sup>2</sup>),

71.8 d (C<sup>10b</sup>), 84.1 d (C<sup>4</sup>), 97.7 s (C<sup>1</sup>), 115.0 d (C<sup>7</sup>), 118.6 d (C<sup>9</sup>), 120.4 s (C<sup>10a</sup>), 127.5 d (C<sup>10</sup>), 127.9 d (C<sup>8</sup>), 143.0 d (C<sup>5</sup>), 144.3 d (C<sup>6</sup>), 144.6 s (C<sup>6a</sup>), 153.2 s and 154.4 s (C<sup>2</sup>, C<sup>3</sup>), 162.5 s and 165.4 s (CO<sub>2</sub>Me). Found, %: C 66.78; H 5.63; N 3.58. C<sub>22</sub>H<sub>23</sub>NO<sub>6</sub>. Calculated, %: C 66.49; H 5.83; N 3.52. *M* 397.43.

**Dimethyl 1-[4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinolin-2-yl]-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (Xa/Xb).** Overall yield 88%. Adduct **Xa**: colorless crystals, mp 140–142°C (from hexane–ethyl acetate), *R<sub>f</sub>* 0.27 (hexane–ethyl acetate, 1:3). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3321 (NH), 1716 (C=O, ester), 1665 (C=O, lactam). Mass spectrum, *m/z* (*I<sub>rel</sub>*, %): 424 (6) [*M*]<sup>+</sup>, 375 (12), 343 (15), 322 (24), 290 (49), 196 (66), 130 (100), 77 (18). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.27 d (1H, 6'-H, *J*<sub>6',5'</sub> = 5.2 Hz), 7.24 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.4, *J*<sub>6',5'</sub> = 5.2 Hz), 7.04 d.d (1H, 7-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>6,7</sub> = 7.6 Hz), 6.82 d (1H, 5-H, *J*<sub>5,6</sub> = 7.6 Hz), 6.68 t (1H, 6-H, *J*<sub>5,6</sub> = *J*<sub>6,7</sub> = 7.6 Hz), 6.60 d (1H, 8-H, *J*<sub>7,8</sub> = 8.0 Hz), 5.72 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.4 Hz), 5.66 br.t (1H, 4-H, *J*<sub>4,3-eq</sub> ≈ *J*<sub>4,3-ax</sub> = 9.1 Hz), 4.34 d.d (1H, 2-H, *J*<sub>2,3-eq</sub> = 5.5, *J*<sub>2,3-ax</sub> = 8.9 Hz), 3.79 s and 3.80 s (3H each, CO<sub>2</sub>Me), 3.14 m and 3.21 m (1H each, 5'-H), 2.51 m (2H, 3'-H), 2.04 m (2H, 3-H), 2.03 m (2H, 4'-H). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 18.2 t (C<sup>43</sup>), 27.5 t (C<sup>3</sup>), 31.4 t (C<sup>33</sup>), 42.2 t (C<sup>53</sup>), 47.8 d (C<sup>4</sup>), 50.1 d (C<sup>2</sup>), 52.5 q and 52.9 q (CO<sub>2</sub>Me), 83.5 d (C<sup>4</sup>), 99.4 s (C<sup>1</sup>), 116.2 d (C<sup>8</sup>), 118.8 d (C<sup>6</sup>), 119.2 s (C<sup>4a</sup>), 126.5 d (C<sup>5</sup>), 128.2 d (C<sup>7</sup>), 142.2 d (C<sup>6</sup>), 144.9 s (C<sup>8a</sup>), 145.4 d (C<sup>5</sup>), 152.3 s and 154.6 s (C<sup>2</sup>, C<sup>3</sup>), 162.4 s and 165.1 s (CO<sub>2</sub>Me), 175.9 s (C<sup>2</sup>). Found, %: C 65.12; H 5.62; N 6.53. C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>. Calculated, %: C 65.08; H 5.70; N 6.60. *M* 424.46.

Adduct **Xb**: colorless crystals, mp 181–182°C (from hexane–ethyl acetate), *R<sub>f</sub>* 0.21 (hexane–ethyl acetate, 1:3). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3325 (NH), 1713 (C=O, ester), 1667 (C=O, lactam). Mass spectrum, *m/z* (*I<sub>rel</sub>*, %): 424 (4) [*M*]<sup>+</sup>, 322 (19), 290 (38), 196 (57), 167 (10), 130 (100), 77 (18), 41 (22). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 7.27 d (1H, 6'-H, *J*<sub>6',5'</sub> = 5.2 Hz), 7.22 d.d (1H, 5'-H, *J*<sub>4',5'</sub> = 1.4, *J*<sub>6',5'</sub> = 5.2 Hz), 7.02 d.d (1H, 7-H, *J*<sub>7,8</sub> = 8.0, *J*<sub>6,7</sub> = 7.6 Hz), 6.82 d (1H, 5-H, *J*<sub>5,6</sub> = 7.6 Hz), 6.68 t (1H, 6-H, *J*<sub>5,6</sub> = *J*<sub>6,7</sub> = 7.6 Hz), 6.59 d (1H, 8-H, *J*<sub>7,8</sub> = 8.0 Hz), 5.72 d (1H, 4'-H, *J*<sub>4',5'</sub> = 1.4 Hz), 5.59 d.d (1H, 4-H, *J*<sub>4,3-eq</sub> = 7.7, *J*<sub>4,3-ax</sub> = 10.7 Hz), 4.23 d.d (1H, 2-H, *J*<sub>2,3-eq</sub> = 4.3, *J*<sub>2,3-ax</sub> = 10.0 Hz), 3.80 s and 3.84 s (3H each, CO<sub>2</sub>Me), 3.14 m and 3.21 m (1H each, 5''-H), 2.51 m (2H, 3''-H), 2.08 m (2H, 3-H), 2.04 m (2H, 4''-H). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 18.0 t (C<sup>43</sup>), 27.5 t (C<sup>3</sup>),

31.2 t (C<sup>33</sup>), 42.0 t (C<sup>53</sup>), 47.5 d (C<sup>4</sup>), 50.6 d (C<sup>2</sup>), 52.3 q and 52.6 q (CO<sub>2</sub>Me), 83.6 d (C<sup>4</sup>), 99.3 s (C<sup>1</sup>), 115.4 d (C<sup>8</sup>), 118.6 d (C<sup>6</sup>), 119.0 s (C<sup>4a</sup>), 126.3 d (C<sup>5</sup>), 128.0 d (C<sup>7</sup>), 141.5 d (C<sup>6</sup>), 144.7 s (C<sup>8a</sup>), 145.5 d (C<sup>5</sup>), 152.2 s and 154.2 s (C<sup>2</sup>, C<sup>3</sup>), 162.3 s and 165.4 s (CO<sub>2</sub>Me), 175.6 s (C<sup>23</sup>). Found, %: C 64.97; H 5.63; N 6.58. C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>. Calculated, %: C 65.08; H 5.70; N 6.60. *M* 424.46.

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