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Reaction of N-Substituted *exo*-2-Hydroxy-5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-*endo*-9-carboxamides with Acetic Acid

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Abstract—Acylation of N-substituted *exo*-2-hydroxy-5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-*endo*-9-carboxamides on heating in boiling glacial acetic acid gave the corresponding *trans*-diacetoxy imides of the norbornane series. The effect of the reaction time on the product composition was studied in the reaction with *exo*-2-hydroxy-*N*-(4-methylphenyl)-5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-*endo*-9-carboxamide. The structure of the resulting norbornane-2,3-dicarboximides was confirmed by IR, ^{1}H NMR, and mass spectra, and the structure of *N*-(2,5-dimethylphenyl)-*exo*-2,*endo*-3-diacetoxybicyclo[2.2.1]heptan-*endo*-5,*endo*-6-dicarboximide was additionally proved by X-ray analysis.

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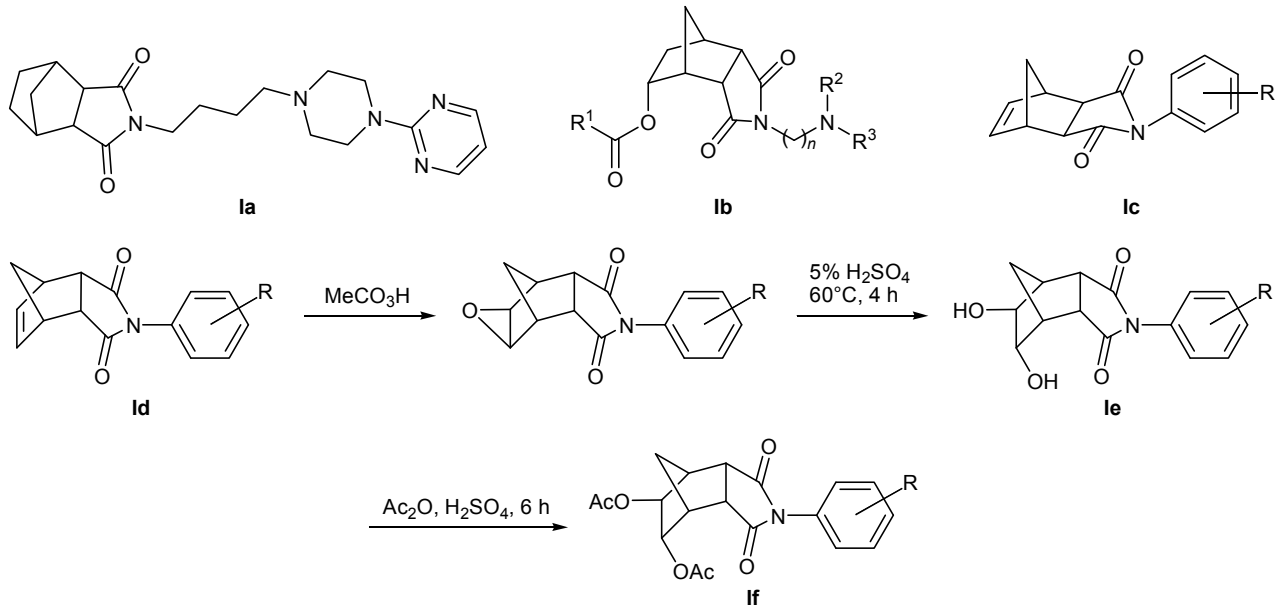
Imides of the norbornane (bicyclo[2.2.1]heptane) series were studied to a considerably lesser extent then their unsaturated analogs. However, these compounds were shown to exhibit anxiolytic and/or antidepressant activity [1]; some imides, e.g., Tandospirone (**Ia**), showed affinity for 5-HT_{1A} and 5-HT_{2A} serotonin receptors [2]. Some imides may be used for the treatment of blood circulation system [3], compounds **Ib**

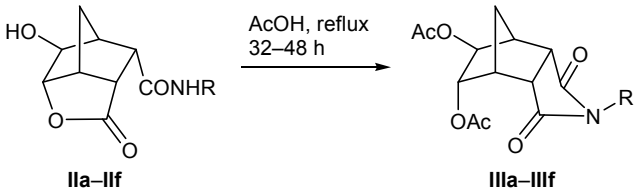
Scheme 1.



R = H, 2-MeO, 3-MeO, 4-MeO, 2-Cl, 3-Cl, 4-Cl, 4-Br, 2-HOCO, 3-HOCO, 4-HOCO.

(R^1 = aryl, hetaryl; R^2, R^3 = alkyl, cycloalkyl; n = 2–4) are antiarrhythmic [4] and sedative agents [5]; they also act as stabilizers against UV irradiation [6]. Stereochemistry of the oxidation of *N*-aryl imides **Ic** and **Id** derived from *endo*- and *exo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acids was examined; it was found that, regardless of the nature and orientation of substituents, the reaction of these compounds with peroxyacetic acid generated *in situ* gave the corresponding epoxy derivatives. The *exo*-oriented oxirane ring was readily opened by the action of 5% aqueous sulfuric acid on heating to produce *trans*-dihydroxy imides **Ie**. The latter were converted into acetates **If** by treatment with acetic anhydride [7] (Scheme 1).

Scheme 2.



IIa–IIf **IIIa–IIIf**

R = 4-MeC_6H_4 (**a**), 2,6-$Me_2C_6H_3$ (**b**), 2,5-$Me_2C_6H_3$ (**c**), 4-BrC_6H_4 (**d**), 4-$MeOC_6H_4$ (**e**), *cyclo*-C_6H_{11} (**f**).

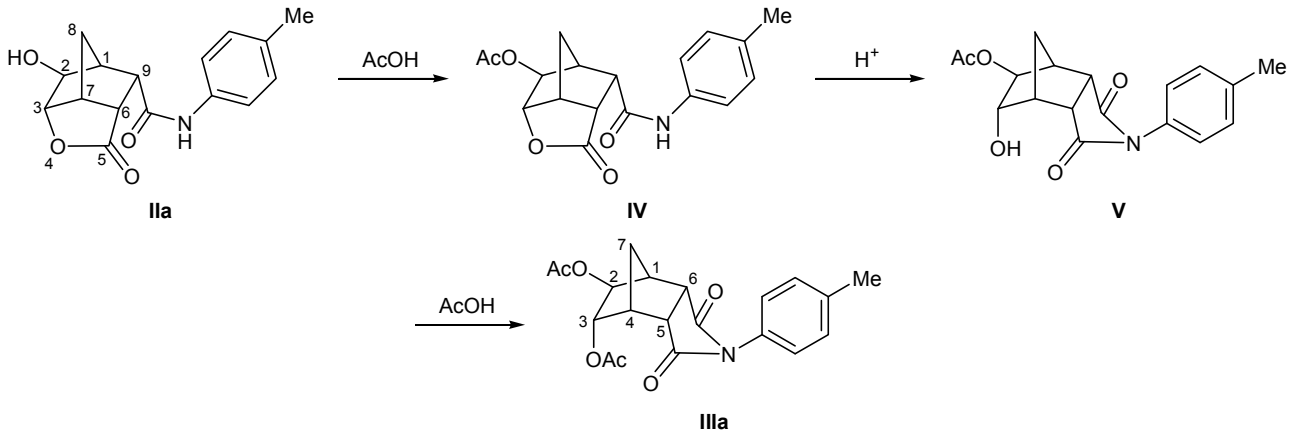
The present work was aimed at developing a new procedure for the synthesis of potentially biologically active *N*-aryl-*exo*-2,*endo*-3-diacetoxybicyclo[2.2.1]-heptane-*endo*-5,*endo*-6-dicarboximides by acylation of the corresponding *N*-aryl-*exo*-2-hydroxy-5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-*endo*-9-carboxamides **IIa**–**IIf** and studying the effect of the reaction time on the product composition. Initial *N*-aryl-*exo*-2-hydroxy-5-oxo-4-oxatricyclo[4.2.1.$0^{3,7}$]nonane-*endo*-9-carboxamides **IIa**–**IIf** were prepared according to the procedures reported in [8]. By heating amides **IIa**–**IIf** in boiling glacial acetic acid over a period of 32–48 h we obtained compounds **IIIa**–**IIIf** (Scheme 2). Imides **IIId** and **IIIe** were described previously [7]; however, their IR and ^{1}H NMR spectra were not given.

Using *N*-(4-tolyl) derivative **IIa** as an example we examined how the reaction time affects the composition of products. The product mixtures were analyzed by thin-layer chromatography and ^{1}H NMR spectroscopy. Scheme 3 illustrates a probable transformation sequence in a simplified form. The compositions of the reaction mixtures, depending on the reaction time, are given in table. These data are consistent with the assumed reaction scheme. In the first step, acylation of the hydroxy group in lactone **IIa** occurs, next follows acid-catalyzed isomerization of acetoxy lactone **IV** into acetoxy imide **V**, and acylation of the *endo*-oriented hydroxy group leads to the final product, *trans*-diacetoxy imide **IIIa** whose fraction sharply increases after heating for 8 h.

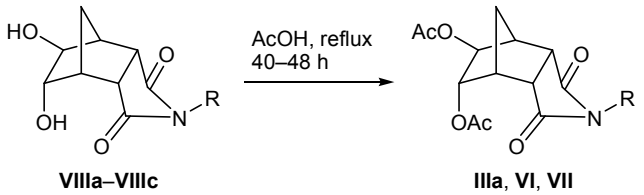
Individual compounds **IIIa** and **IV** were isolated by column chromatography on silica gel from the reaction mixture obtained in run no. 4. We also isolated a fraction (21%) containing amido lactone **IV** and intermediate **V**. The latter was not detected in the reaction mixture by NMR spectroscopy; presumably, it was formed as a result of unexpected isomerization of compound **IV** during chromatography. By special experiments we showed that pure acetoxy lactone **IV** is converted into final product **IIIa** in 91% yield on heating in boiling acetic acid over a period of 26 h. Diacetates **IIIa**, **VI**, and **VII** were also synthesized by independent method, by reaction of *trans*-dihydroxy imides **VIIIa**–**VIIIc** [8] with acetic acid (Scheme 4).

The structure of *trans*-diacetoxy imide **IIIa** was additionally confirmed by its transformation into

Scheme 3.



Scheme 4.



VIIIa–VIIIc **IIIa**, **VI**, **VII**

VI, **VIIIa**, R = H; **VII**, **VIIIb**, R = Me;
IIIa, **VIIIc**, R = 4-MeC_6H_4.

known acid **IX** [9] on heating in 10% aqueous sodium carbonate, followed by treatment with hydrochloric acid. Acylation of the *exo*-oriented hydroxy group in carboxylic acid **IX** was accomplished by heating in boiling glacial acetic acid. Compound **X** thus obtained (Scheme 5) was reported previously [10], but neither its properties nor spectral parameters were given.

The molecular and crystalline structures of compound **IIIc** were determined by X-ray analysis (see figure). The five-membered $C^1C^2C^3C^7C^6$ and $C^3C^4C^5C^6C^7$ rings in molecule **IIIc** have an *envelope* conformation with the C^7 atom deviating by 0.877 and 0.896 Å, respectively, from the planes formed by the other atoms in the above rings. The six-membered $C^1C^2C^3C^4C^5C^6$ ring adopts a *boat* conformation with the following puckering parameters [11]: S = 1.13, θ = 87.4°, ψ = 1.6°. Such configuration of the cage-like fragment in imide **IIIc** is typical of analogous compounds [12, 13].

The substituent on C^1 occupies *exo* position, and the substituent on C^2 is oriented *endo*; the torsion angles $C^3C^2C^1O^5$ and $C^6C^1C^2O^3$ are 120.5(3) and 128.0(3)°, respectively. The *endo* orientation of the acetoxy group on C^2 is responsible for shortened intramolecular contact $O^3\cdots C^8$ 2.71 Å (the sum of the corresponding van der Waals radii is 3.00 Å [14]). The heterocyclic fragment is oriented *endo* relative to the bicyclic skeleton [the torsion angle $C^6C^4C^5C^9$ is –124.1(2)°]. The imide nitrogen atom has a planar–trigonal bond configuration [the sum of the bond angles at the nitrogen atom is 360(1)°], as in analogous structures [12, 13]. The N^1–C^{14} bond length is 1.429(5) Å, which is typical of unconjugated bonds (average bond length 1.426 Å [15]), and the aryl group is turned through an angle of 81.3(5)° [torsion angle $C^8N^1C^{14}C^{15}$] with respect to the heteroring, indicating the absence of conjugation between the imide fragment and the aromatic ring. Molecules **IIIc** in crystal are characterized by disordering of the aryl fragment by two positions with equal populations due to rotation about the N^1–C^{14} bond.

Reaction of amido lactone **IIa** with acetic acid

Run no.	Reaction time, h	Composition of products,[a] %		
		IV	**V**	**IIIa**
1	4	46[b]	0	0
2	6	51	49	0
3	8	67	33	0
4	16	37	0	63
5	24	13	0	87
6	32	0	0	100

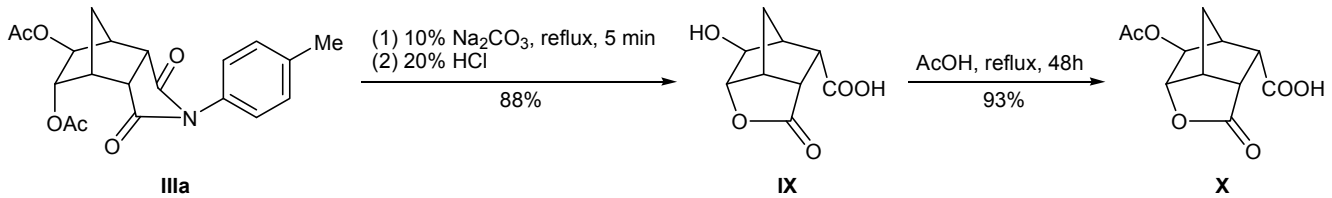
[a] According to the ^{1}H NMR data.
[b] The reaction mixture also contained 54% of initial amido lactone **IIa**.

The structure of the other compounds was confirmed by their IR and ^{1}H NMR spectra. In the IR spectra of **IIIa**–**IIIf**, **VI**, and **VII**, the imide fragment gave rise to absorption bands at 1777–1735 and 1735–1705 cm^{-1} belonging to symmetric and antisymmetric stretching vibrations of the carbonyl groups; the low-frequency band had considerably higher intensity [16].

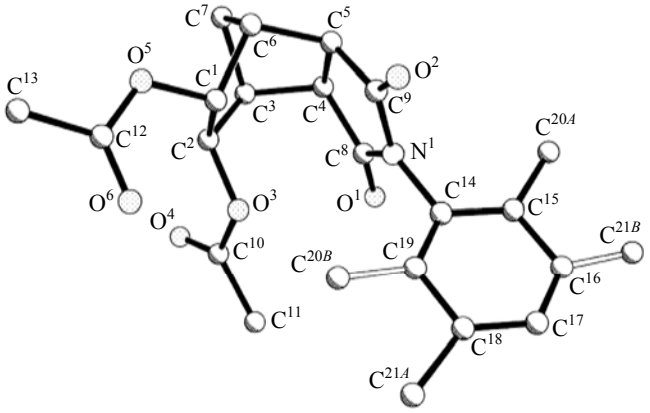
The ^{1}H NMR spectra of lactones **IV** and **X** were characterized by similar positions of signals from protons in the bicyclic skeleton. The amide NH proton signal in the spectrum of **IV** was located at δ 10.07 ppm, and compound **X** displayed a singlet from the carboxy proton at δ (12.85 ppm.

The ^{1}H NMR spectra of **IIIa**–**IIIf**, **VI**, and **VII** contained some characteristic signals: a doublet from 1-H at δ 2.62–2.75 ppm ($^3J_{1,6}$ = 5.3–6.0 Hz), a singlet from *endo*-2-H at δ 4.36–4.88 ppm, and a signal from *exo*-3-H at δ 4.77–4.91 ppm. The latter signal appears

Scheme 5.



IIIa **IX** **X**



Structure of the molecule of *N*-(2,5-dimethylphenyl)-*exo*-2,*endo*-3-diacetoxybicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (**IIIc**) according to the X-ray diffraction data.

in the spectrum of **VII** as a doublet as a result of coupling with 4-H with a coupling constant J of 5.1 Hz. In the ^{1}H NMR spectra of the other compounds, the *exo*-3-H proton resonates as a broadened singlet. Signals from nonequivalent *exo*-protons on C^5 and C^6 were located in the region δ 3.12–3.73 ppm, and the difference between their chemical shifts was Δδ = 0.16–0.36 ppm. Methyl protons in the *exo*- and *endo*-oriented acetoxy groups resonated at δ 2.00–2.03 and 1.68–1.88 ppm, respectively, which is very consistent with published data for structurally related compounds [17]. The ^{1}H NMR spectrum of monoacetoxy imide **V** showed a different mutual arrangement of the 2-H and 3-H signals (δ 4.38 and 4.33 ppm, respectively) than in the spectra of diacetoxy derivatives **IIIa**–**IIIf**, **VI**, **VII**. In addition, the spectrum of **V** contained a doublet from the hydroxy proton at δ 5.56 ppm (^3J = 3.9 Hz). The spectra of compounds **IIIa**–**IIIf** and **V**–**VII** also contained complete sets of signals from the *N*-aryl imide fragment.

EXPERIMENTAL

The IR spectra were recorded in KBr on UR-20 and Paragon 500 FT-IR spectrometers. The ^{1}H NMR spectra were measured on a Varian VXR spectrometer at 300 MHz from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectrum (electron impact, 70 eV) was obtained on a Varian 1200L instrument. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using diethyl ether (A) or propan-2-ol (B) as eluent; development with iodine vapor. The elemental compositions were determined on a Carlo Erba analyzer.

X-Ray diffraction data for compound IIIc. Monoclinic crystals, $C_{21}H_{21}NO_6$, with the following unit cell parameters (at 20°C): a = 26.962(4), b = 7.8475(7), c = 23.744(6) Å; β = 124.52(2)°; V = 4139(1) Å^3; M 383.39; Z = 8; space group $C2/c$; d_{calc} = 1.230 g/cm^3; μ(MoK_α) = 0.091 mm^{-1}; F(000) = 1616. The unit cell parameters and intensities of 14825 reflections (6883 of which were independent with R_{int} = 0.092) were measured on an Xcalibur-3 diffractometer (MoK_α irradiation, CCD detector, graphite monochromator, ω scanning, $2\theta_{max}$ = 50°). The structure was solved by the direct method using SHELXTL software package [18]. The C^{15}–C^{20A}, C^{16}–C^{21B}, C^{19}–C^{20B}, and C^{18}–C^{21A} bond lengths in the disordered fragment were restricted to 1.506(5) Å in the refinement procedure. The positions of hydrogen atoms were determined on the basis of geometry considerations and were refined according to the riding model with $U_{iso} = nU_{eq}$ (n = 1.5 for methyl groups; n = 1.2 for other hydrogen atoms). The structure was refined by F^2 using full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms to wR_2 = 0.189 (for 3282 reflections) and R_1 = 0.066 [for 1268 reflections with $F > 4\sigma(F)$], S = 0.84. The complete set of crystallographic data, including coordinates of atoms, was deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 721245).

***trans*-Diacetoxy imides IIIa–IIIf, VI, and VII (*general procedure*).** A solution of 2 mmol of amido lactone **IIa**–**IIf** or *trans*-dihydroxy imide **VIIIa**–**VIIIc** in 15 ml of glacial acetic acid was heated under reflux until the reaction was complete (TLC, 32–48 h). The solvent was distilled off under reduced pressure, and the residue was purified by recrystallization from propan-2-ol.

***exo*-2,*endo*-3-Diacetoxy-*N*-(4-methylphenyl)bicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIIa).** Yield 0.65 g (88%), mp 191–193°C, R_f 0.33 (diethyl ether). IR spectrum, ν, cm^{-1}: 2990, 1735, 1710, 1520, 1390, 1240, 1195, 1060, 1040. ^{1}H NMR spectrum, δ, ppm: 1.69 s (3H, *endo*-AcO), 1.77 d (1H, *anti*-7-H, ^2J = 11.3 Hz), 1.97 d (1H, *syn*-7-H), 2.03 s (3H, *exo*-AcO), 2.35 s (3H, CH_3), 2.73 d (1H, 1-H, $^3J_{1,6}$ = 5.7 Hz), 3.05 m (1H, 4-H), 3.33 d.d (1H, 5-H, $^3J_{4,5}$ = 5.1, $^3J_{5,6}$ = 9.9 Hz), 3.55 d.d (1H, 6-H), 4.65 s (1H, 2-H), 4.88 br.s (1H, 3-H), 7.12 d (2H, H_{arom}), 7.33 d (2H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 371 (44.5) $[M]^+$, 372 (8.5) $[M + 1]^+$, 329 (6.9), 286 (18.2), 269 (14.9), 241 (21.6), 206 (17.7), 108 (29.2), 107 (100), 79 (45.8). Found, %: C 64.77; H 5.61; N 3.89. $C_{20}H_{21}NO_6$. Calculated, %: C 64.68; H 5.70; N 3.77.

***exo*-2,*endo*-3-Diacetoxy-*N*-(2,6-dimethylphenyl)-bicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIIb).** Yield 0.60 g (78%), mp 210–212°C, R_f 0.62 (diethyl ether). IR spectrum, ν, cm^{-1}: 3005, 1740, 1710, 1485, 1370, 1245, 1230, 1190, 1050. ^1H NMR spectrum, δ, ppm: 1.73 s (3H, *endo*-AcO), 1.77 d (1H, *anti*-7-H, ^2J = 11.4 Hz), 2.00 s (3H, *exo*-AcO), 2.02 d (1H, *syn*-7-H), 2.04 s (3H, CH_3), 2.28 s (3H, CH_3), 2.75 d (1H, 1-H, $^3J_{1,6}$ = 5.4 Hz), 3.11 m (1H, 4-H), 3.52 d.d (1H, 5-H, $^3J_{4,5}$ = 4.7, $^3J_{5,6}$ = 10.3 Hz), 3.73 d.d (1H, 6-H), 4.88 s (1H, 2-H), 4.89 d (1H, 3-H, $^3J_{3,4}$ = 5.1 Hz), 7.16–7.28 (3H, H_{arom}). Found, %: C 65.31; H 6.13; N 3.72. $C_{21}H_{23}NO_6$. Calculated, %: C 65.44; H 6.02; N 3.63.

***exo*-2,*endo*-3-Diacetoxy-*N*-(2,5-dimethylphenyl)-bicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIIc).** Yield 0.64 g (83%), mp 170–172°C, R_f 0.64 (diethyl ether). IR spectrum, ν, cm^{-1}: 2968, 2924, 1777, 1744, 1709, 1509, 1420, 1368, 1238, 1186, 1065, 1038, 1017. ^1H NMR spectrum, δ, ppm: 1.76 s (3H, *endo*-AcO), 1.97 d (1H, *anti*-7-H, ^2J = 10.4 Hz), 2.01 s (3H, *exo*-AcO), 2.02 s (3H, CH_3), 2.23 d (1H, *syn*-7-H), 2.28 s (3H, CH_3), 2.73 d (1H, 1-H, $^3J_{1,6}$ = 6.0 Hz), 3.06 m (1H, 4-H), 3.50 d.d (1H, 5-H, $^3J_{4,5}$ = 5.7, $^3J_{5,6}$ = 9.9 Hz), 3.66 d.d (1H, 6-H), 4.66 s (1H, 2-H), 4.91 br.s (1H, 3-H), 6.90–6.96 (1H, H_{arom}), 7.10–7.26 (2H, H_{arom}). Found, %: C 65.51; H 6.10; N 3.59. $C_{21}H_{23}NO_6$. Calculated, %: C 65.44; H 6.02; N 3.63.

***exo*-2,*endo*-3-Diacetoxy-*N*-(4-bromophenyl)bicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIId).** Yield 0.61 g (70%), mp 208–210°C; published data [7]: mp 133–134°C; R_f 0.66 (propan-2-ol). IR spectrum, ν, cm^{-1}: 2956, 1740, 1714, 1492, 1375, 1239, 1044. ^1H NMR spectrum, δ, ppm: 1.68 s (3H, *endo*-AcO), 1.79 d (1H, *anti*-7-H, ^2J = 11.4 Hz), 1.97 d (1H, *syn*-7-H), 2.03 s (3H, *exo*-AcO), 2.74 d (1H, 1-H, $^3J_{1,6}$ = 6.0 Hz), 3.06 m (1H, 4-H), 3.35 d.d (1H, 5-H, $^3J_{5,6}$ = 10.1 Hz), 3.57 d.d (1H, 6-H), 4.63 s (1H, 2-H), 4.90 br.s (1H, 3-H), 7.22 d (2H, H_{arom}), 7.76 d (2H, H_{arom}).

***exo*-2,*endo*-3-Diacetoxy-*N*-(4-methoxyphenyl)bicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIIe).** Yield 0.59 g (76%), mp 123–125°C; published data [7]: mp 132–134°C; R_f = 0.27 (diethyl ether). IR spectrum, ν, cm^{-1}: 2990, 1740, 1710, 1610, 1520, 1450, 1380, 1310, 1250, 1195, 1060, 1040. ^1H NMR spectrum, δ, ppm: 1.71 s (3H, *endo*-AcO), 1.77 d (1H, *anti*-7-H, ^2J = 11.0 Hz), 1.97 d (1H, *syn*-7-H), 2.03 s (3H, *exo*-AcO), 2.73 d (1H, 1-H, $^3J_{1,6}$ = 5.8 Hz), 3.05 m (1H, 4-H), 3.31 d.d (1H, 5-H, $^3J_{4,5}$ = 5.0, $^3J_{5,6}$ = 9.8 Hz), 3.54 d.d (1H, 6-H), 3.79 s (3H, OCH_3), 4.64 s (1H, 2-H), 4.87 br.s (1H, 3-H), 7.07 d (2H, H_{arom}), 7.16 d (2H, H_{arom}).

***exo*-2,*endo*-3-Diacetoxy-*N*-cyclohexylbicyclo-[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (IIIf).** Yield 0.66 g (91%), mp 98–100°C, R_f 0.79 (diethyl ether). IR spectrum, ν, cm^{-1}: 2950, 1745, 1705, 1380, 1245, 1200, 1060. ^1H NMR spectrum, δ, ppm: 1.11–1.31 (3H, C_6H_{11}), 1.54–1.68 (5H, C_6H_{11}), 1.78 d (1H, *anti*-7-H), 1.88 s (3H, *endo*-AcO), 1.90 d (1H, *syn*-7-H), 2.00 s (3H, *exo*-AcO), 2.00–2.10 (2H, C_6H_{11}), 2.62 d (1H, 1-H, $^3J_{1,6}$ = 5.9 Hz), 2.98 m (1H, 4-H), 3.12 d.d (1H, 5-H, $^3J_{4,5}$ = 5.1, $^3J_{5,6}$ = 9.6 Hz), 3.30 d.d (1H, 6-H), 3.83 t.t (1H, NCH), 4.45 s (1H, 2-H), 4.78 br.s (1H, 3-H). Found, %: C 62.72; H 6.81; N 3.96. $C_{19}H_{25}NO_6$. Calculated, %: C 62.80; H 6.93; N 3.85.

***exo*-2,*endo*-3-Diacetoxybicyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (VI).** Yield 0.51 g (90%), oily substance, R_f 0.18 (diethyl ether). IR spectrum, ν, cm^{-1}: 3291, 2933, 1744, 1700, 1372, 1238, 1050. ^1H NMR spectrum, δ, ppm: 1.71 d (1H, *anti*-7-H, ^2J = 10.5 Hz), 1.88 s (3H, *endo*-AcO), 1.90 d (1H, *syn*-7-H), 2.00 s (3H, *exo*-AcO), 2.62 d (1H, 1-H, $^3J_{1,6}$ = 5.3 Hz), 2.97 m (1H, 4-H), 3.12 d.d (1H, 5-H, $^3J_{4,5}$ = 5.0, $^3J_{5,6}$ = 9.7 Hz), 3.30 d.d (1H, 6-H), 4.45 s (1H, 2-H), 4.77 br.s (1H, 3-H), 7.70 s (1H, NH). Found, %: C 55.42; H 5.49; N 5.01. $C_{13}H_{15}NO_6$. Calculated, %: C 55.51; H 5.38; N 4.98.

***exo*-2,*endo*-3-Diacetoxy-*N*-methylbicyclo[2.2.1]-heptane-*endo*-5,*endo*-6-dicarboximide (VII).** Yield 0.58 g (98%), mp 149–151°C, R_f 0.24 (diethyl ether). IR spectrum, ν, cm^{-1}: 2980, 1770, 1735, 1710, 1435, 1380, 1280, 1245, 1045. ^1H NMR spectrum, δ, ppm: 1.71 d (1H, *anti*-7-H, ^2J = 10.5 Hz), 1.88 s (3H, *endo*-AcO), 1.92 d (1H, *syn*-7-H), 2.00 s (3H, *exo*-AcO), 2.63 d (1H, 1-H, $^3J_{1,6}$ = 6.0 Hz), 2.85 s (3H, NCH_3), 2.97 m (1H, 4-H), 3.16 d.d (1H, 5-H, $^3J_{4,5}$ = 5.0, $^3J_{5,6}$ = 9.7 Hz), 3.42 d.d (1H, 6-H), 4.36 s (1H, 2-H), 4.77 d (1H, 3-H, $^3J_{3,4}$ = 5.1 Hz). Found, %: C 57.01; H 5.71; N 4.61. $C_{14}H_{17}NO_6$. Calculated, %: C 56.94; H 5.80; N 4.74.

***exo*-2-Acetoxy-*N*-(4-methylphenyl)-5-oxo-4-oxatricyclo[4.2.1.0^{3,7}]nonane-*endo*-9-carboximide (IV).** A solution of 1.15 g (4 mmol) of amido lactone **IIa** in 15 ml of glacial acetic acid was heated for 16 h under reflux. The solvent was removed under reduced pressure, and the residue was passed through a column charged with silica gel (substrate-to-sorbent ratio 1:150; eluent diethyl ether). The first fraction con-

tained compound **IIIa**, yield 0.98 g (70%), R_f 0.33 (diethyl ether). The second fraction was a mixture of compound **IV** and *exo*-2-acetoxy-*endo*-3-hydroxy-*N*-(4-methylphenyl)bi-cyclo[2.2.1]heptane-*endo*-5,*endo*-6-dicarboximide (**V**) (48 and 52%, respectively, according to the ^{1}H NMR data), yield 0.29 g (21%), R_f 0.10 (diethyl ether). The third fraction contained compound **IV**, yield 0.13 g (9%), mp 214–216°C, R_f 0.10 (diethyl ether). IR spectrum, ν, cm^{-1}: 2950, 1765, 1675, 1030. ^{1}H NMR spectrum, δ, ppm: 1.62 d (1H, *anti*-8-H, ^2J = 11.3 Hz), 1.93 d (1H, *syn*-8-H), 2.02 s (3H, *exo*-AcO), 2.25 s (3H, CH_3), 2.64 br.s (1H, 1-H), 2.78 d.d (1H, 6-H, $^3J_{6,7}$ = 4.5, $^3J_{6,9}$ = 10.2 Hz), 3.13 d.d (1H, 9-H, $^3J_{1,9}$ = 3.5 Hz), 3.32 m (1H, 7-H), 4.58 d (1H, 3-H, $^3J_{3,7}$ = 4.8), 5.38 s (1H, 2-H), 7.10 d (2H, H_{arom}), 7.41 d (2H, H_{arom}), 10.07 br.s (1H, NH). Found, %: C 65.71; H 5.75; N 4.33. $C_{18}H_{19}NO_5$. Calculated, %: C 65.64; H 5.81; N 4.25.

Independent synthesis of compound (IIIa). A solution of 0.66 g (2 mmol) of compound **IV** in 15 ml of glacial acetic acid was heated for 26 h under reflux. The solvent was removed under reduced pressure, and the product was purified by recrystallization from propan-2-ol. Yield 0.68 g (91%).

***exo*-2-Hydroxy-5-oxo-4-oxatricyclo[4.2.1.0^{3,7}]-nonane-*endo*-9-carboxylic acid (IX).** A suspension of 0.74 g (2 mmol) of compound **IIIa** in 10 ml of 10% aqueous sodium carbonate was heated for 5 min at the boiling point until a transparent solution was formed. The mixture was acidified by adding dropwise 20% hydrochloric acid until a weakly acidic reaction according to litmus. Volatile substances were removed under reduced pressure, the residue was treated with 12 ml of boiling acetone, the mixture was filtered while hot, the filtrate was cooled, and the precipitate was filtered off, washed on a filter with a small amount of acetone, and dried in air. Yield 0.35 g (88%), mp 200–202°C; published data [9]: mp 202–203°C.

***exo*-2-Acetoxy-5-oxo-4-oxatricyclo[4.2.1.0^{3,7}]-nonane-*endo*-9-carboxylic acid (X).** A solution of 0.40 g (2 mmol) of compound **IX** in 15 ml of glacial acetic acid was heated under reflux until the reaction was complete (TLC, 48 h). The solvent was removed under reduced pressure, and the product was purified by recrystallization from propan-2-ol. Yield 0.45 g (93%), mp 113–115°C, R_f 0.12 (diethyl ether), 0.40 (propan-2-ol). IR spectrum, ν, cm^{-1}: 3320, 1780, 1735, 1420, 1380, 1270, 1170, 1040. ^{1}H NMR spectrum, δ, ppm: 1.66 d (1H, *anti*-8-H, ^2J = 11.6 Hz), 1.88 d (1H, *syn*-8-H), 2.03 s (3H, *exo*-AcO), 2.59 br.s (1H, 1-H), 2.77 d.d (1H, 6-H, $^3J_{6,7}$ = 4.7, $^3J_{6,9}$ = 11.0 Hz), 3.13 d.d (1H, 9-H, $^3J_{1,9}$ = 3.5 Hz), 3.29 m (1H, 7-H), 4.57 d (1H, 3-H, $^3J_{3,7}$ = 5.1 Hz), 5.09 s (1H, 2-H), 12.85 br.s (1H, COOH).

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