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PREPARATION AND STRUCTURE OF *DIEXO*-OXANORBORNANE-FUSED 1,3-HETEROCYCLES

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Dedicated to professor Gábor Bernáth on the occasion of his 70th birthday

Abstract – *Via* the reaction of *diexo*-oxanorbornanedicarboxylic anhydride with toluene, the *diexo*-aroylcarboxylic acid (**3a**) was prepared, which exists partly as the tautomeric lactol (**3b**). With bifunctional reagents, **3a** yields fused heterocycles containing three–six rings. Thus, alkylenediamines result in imidazole- and 1,3-diazepine-fused oxygen-bridged isoindolones (**6a,b**), alkanolamines form the oxazole- and 1,3-oxazine-fused oxanorbornene derivatives (**7a-c**), and *o*-phenylenediamine undergoes cyclization to furnish the condensed benzimidazole (**8**). The reaction of **3a** with *diexo*-aminonorbornanecarbohydrazide yields a pyrimidopyridazine containing six condensed rings (**9**). In a similar reaction with *diendo*-aminonorbornenecarbohydrazide, cyclopentadiene cleaves off to give the tricyclic retro Diels-Alder product (**10**). The structures, and particulary the configurations at the oxanorbornane ring systems and the position of the aryl substituent, were established by means of 1D- and 2D-NMR spectroscopy and, for **3b** and **7c**, also by X-Ray measurements.

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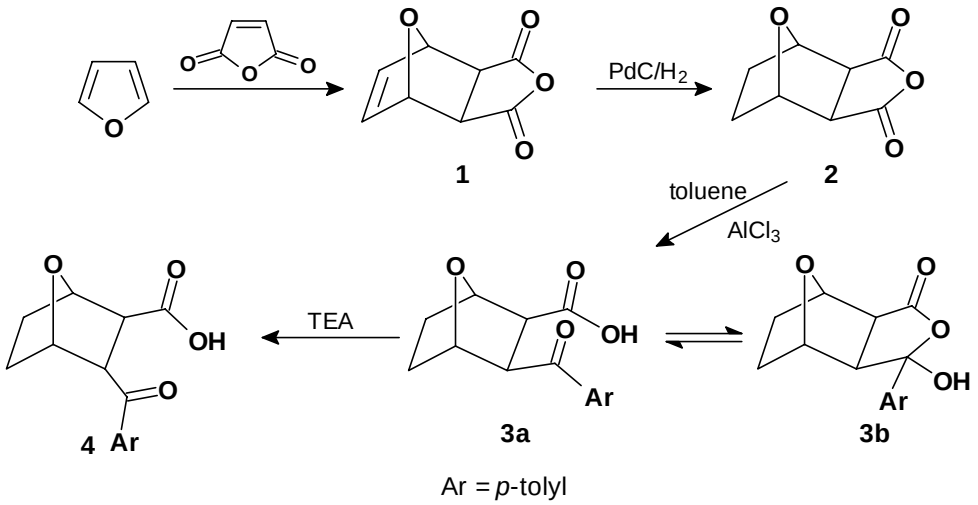
1. INTRODUCTION

Diendo- and *diexo*-3-aminobicyclo[2.2.1]hept-5-ene-2-carboxylic acids and derivatives have been used to prepare 1,3-heterocycles.[1,2] From stereoisomeric bicyclo[2.2.1]heptane-2,3-dicarboxylic anhydrides, aroylcarboxylic acids have been prepared and applied for the synthesis of new hetero compounds containing the partly saturated condensed methylene-bridged isoindolone unit.[3,4] We now extend the synthetic work to the isomeric *diexo*-oxanorbornane derivatives. The target of this activity is to prepare them from the previously unknown *diexo*-3-aroyl-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid (**3a**) as starting compound. Besides the chemical and stereochemical features of the fused-skeleton saturated heterocycles, they are of importance from pharmacological aspects because similar compounds possess an anorectic effect and are applied in therapy.[5,6] Chiral perhydrobenzoxazines containing a furan ring earlier served as nitrogen source and chiral inductor in the stereoselective synthesis of enantiopure decahydro-isoquinolines.[7] Furan has been applied as a diene in an intramolecular Diels-Alder reaction for the synthesis of 1,4-epoxycadinane,[8] in high-pressure reactions,[9] in tandem intramolecular/radical cyclization[10] and to build an oxygen bridge into various molecules.[11]

2. RESULTS AND DISCUSSION

2.1. PREPARATIONS

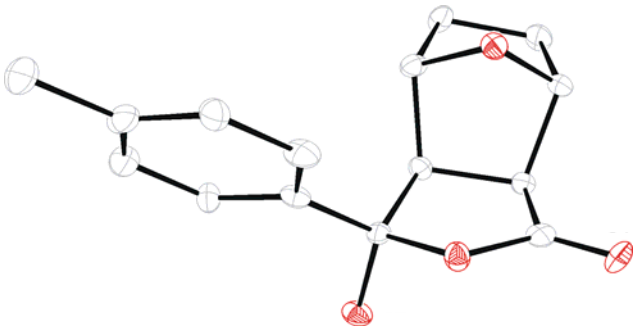
The reaction of furan with maleic acid anhydride results in 7-oxabicyclo[2.2.1]hept-5-ene-1,2-dicarboxylic anhydride (**1**),[12-14] which was reduced to the saturated derivative (**2**)[15] and then transformed with toluene/$AlCl_3$ to *diexo*-3-*p*-toluoyl-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid (**3a**) (Scheme 1).



Scheme 1

Compound (**3a**) exists as a mixture with its cyclo tautomer (**3b**), which was isolated from the ethanolic solution and the structure proved by means of an X-Ray method (Figure 1). The lactol containing a CCl_3

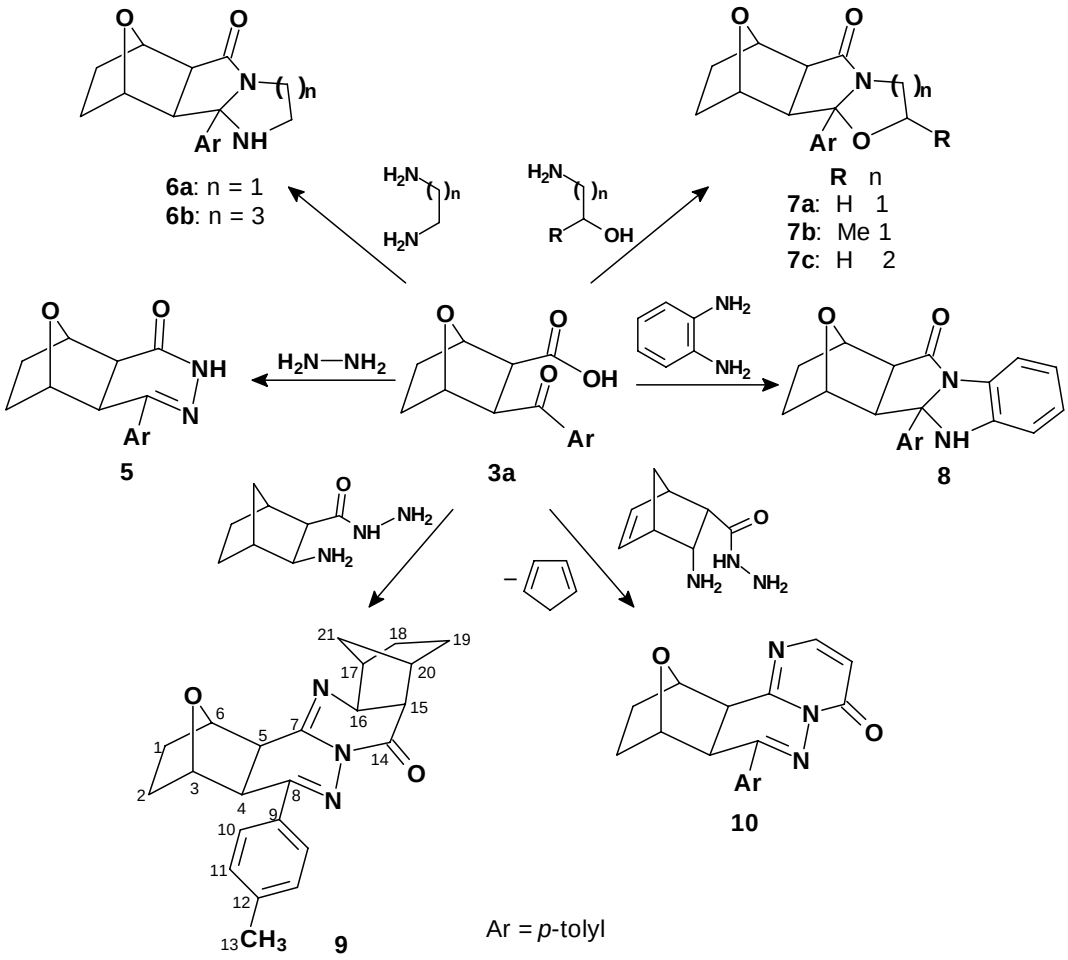
group instead of aryl were already prepared from **2** with trichloroacetate.[16] Owing to facile enolization of the aryl group, **3a** isomerizes with triethylamine to **4**.



Perspective view of **3b**.
Thermal ellipsoids have been drawn
at a probability level of 30%

Figure 1

From **3a** and hydrazine, the oxanorbornane-condensed pyridazinone (**5**) is formed (Scheme 2). Refluxing **3a** in toluene with ethylenediamine and 1,4-diaminobutane furnishes the tetracyclic imidazo (**6a**) and 1,3-diazepino *diexo*-condensed epoxyisoindolones (**6b**).



Scheme 2

The reactions of **3a** with aminoethanol and aminopropanols yield the oxazole- (**7a**), (**7b**) and 3,1-oxazine-fused epoxyisoindolones (**7c**), while from **3a** with phenylenediamine, the condensed pentacyclic benz-imidazole (**8**) is formed.

With *diexo*-3-aminobicyclo[2.2.1]heptane-2-carbohydrazide, **3a** cyclizes to the condensed hexacyclo derivative (**9**) containing a central pyrimidopyridazine, one *diexo*-condensed norbornane and one oxanorbornane unit. In reaction with the isomeric *diendo*-3-aminobicyclo[2.2.1]hept-5-ene-2-carbohydrazide, **3a** yields the fused pyrimidopyridazine (**10**) because cyclopentadiene splits off. The reaction is explained by the presence of the double bond in the norbornane moiety, which allows a ready thermal decomposition to give cyclopentadiene and **10** in retro Diels-Alder reaction.

2.2. STRUCTURE DETERMINATIONS BY NMR SPECTRAL MEASUREMENTS AND QUANTUM CHEMICAL CALCULATIONS

The structures of the new compounds follow from the NMR spectroscopic data. The H,H connectivities could be concluded from the H,H-COSY spectra; direct and long-range C,H coupling information was obtained from HMQC and HMBC. NOESY spectra was also recorded to find the spatially adjacent protons. The crucial stereochemistry, *i.e.* the *exo* or *endo* configurations of the substituents/annelated rings on the oxanorbornane skeleton in all compounds and the position of the *p*-tolyl group in **5-7**, were also established. For the assignment of this stereochemistry, a number of unequivocal NMR spectroscopic criteria are available.

(*i*) The *vicinal* H-5–H-6 and H-3–H-4 coupling constants are strongly dependent on the *exo/endo* positions of H-4,-5: $J_{\text{H-3, H-4-}exo} \sim 5$ Hz, but $J_{\text{H-3, H-4-}endo} < 0.1$ Hz (see the spectroscopic numbering used in the NMR part on **9** in Scheme 2).[17] Accordingly, H,H cross-peaks are present or not in the corresponding H,H-COSY NMR spectra.

(*ii*) Between H-1-*exo* and H-5-*exo*, a long-range W coupling of ~2.5 Hz can be found[17] (indicated by the corresponding cross-peak in the H,H-COSY NMR spectra); the corresponding *exo/endo* coupling proved negligible;[17] hence, no cross-peak was observed in the H,H-COSY NMR spectra.

(*iii*) NOE between the *endo* protons in positions 1,5 and 2,4 proved useful for assigning the *exo* or *endo* configuration of the substituents. If only the *exo* proton is present (*endo* substitution), the corresponding NOE can not be obtained as a cross-peak in the 2D NOESY NMR spectra.

With these criteria, the *exo* or *endo* configuration of the compounds was established. Thus, 4-*endo*,5-*exo* substitution was found for **4**, while for **5**, **7c** and **8-10** *diexo* 4,5-annelation was proved. Compounds (**3a,b**) exist as a mixture in solution, and the equilibrium does not allow establishment of the configuration of the oxanorbornane moiety.

For establishment of the position of the aryl in **6-8,** the NOEs was applied. A number of NOE enhancements were found in the 2D NOESY NMR spectra, but these were not suitable for discrimination of the C-8 configuration. In contrast, the ring current effect of the aryl was really useful. The method for application the ring current effect of the nearby aromatic ring for determination of the disposition of the protons is known.[18-20] Thus, the *trans* configuration of the aryl and H-4-*endo* causes a strong shielding

effect on H-3, but in the *cis* case only a very small ring current effect on H-3 can be expected. These expectations are in complete concordance with the experimental ^{1}H chemical shifts: whereas H-3 is strongly shielded (δ ~3.65 ppm) in **6b** and **7c**, obviously because of the ring current effect, the same proton resonates with the normal value (δ 4.90-5.20 ppm) in **4**, **5**, **8** and **10**. In the latter cases, the aryl substituent is remote (*trans*) from H-3, and the corresponding ring current effect therefore remains small. To confirm these conclusions from model structures, the aryl and H-4-*endo cis/trans* isomers of **7c** were *ab initio* MO calculated, and the corresponding ^{1}H chemical shift of H-3 in the two isomers was determined by the GIAO method. The results are depicted in Figure 2.

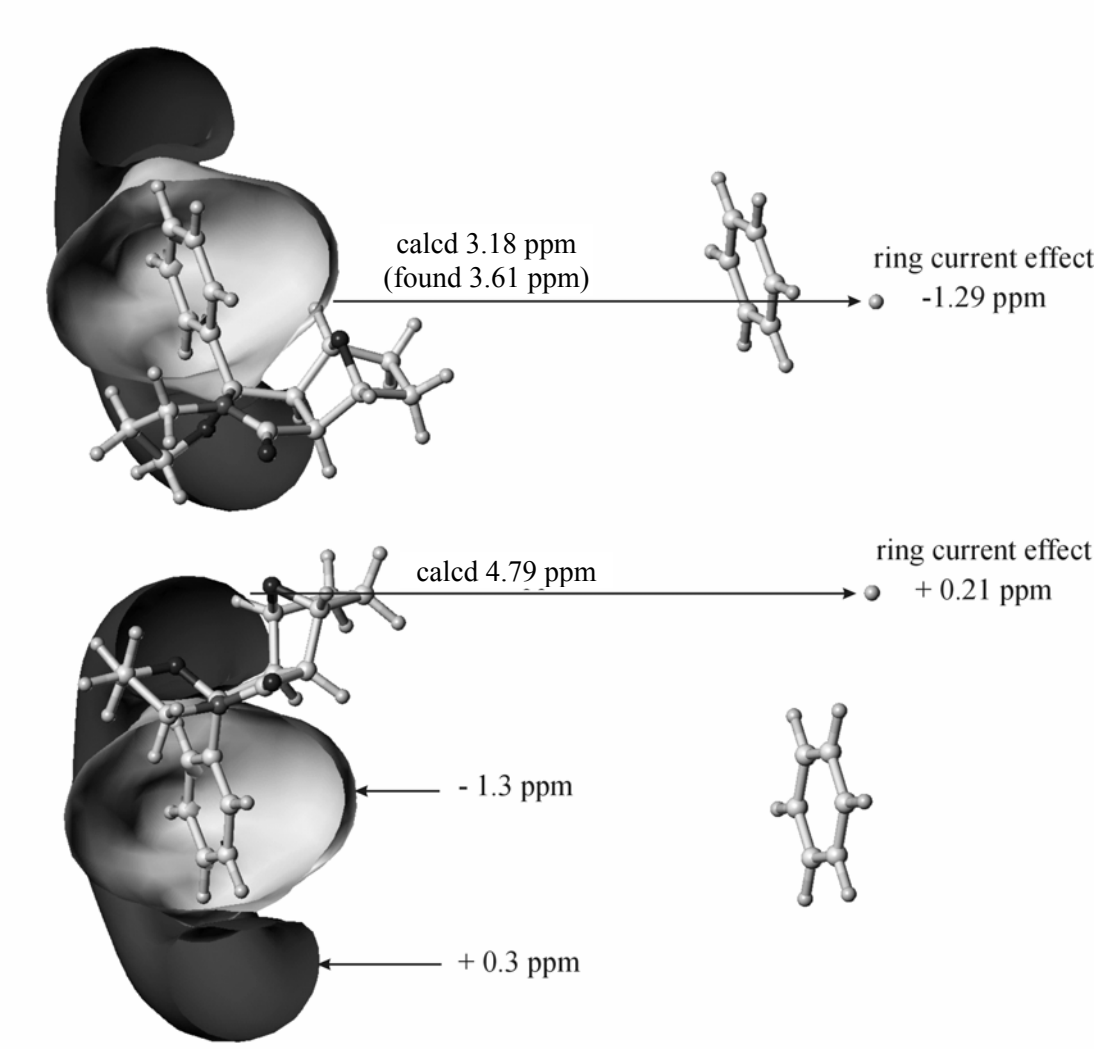
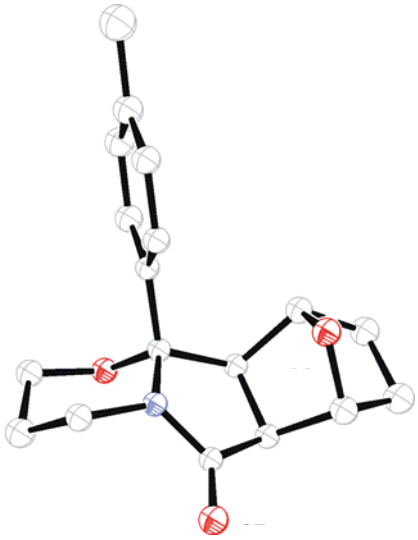


Figure 2

Ring current effect on H-3 in **7c**

Both the chemical shift of H-3 (δ = 3.18 ppm) and the ring current effect of the aryl on H-3 (–1.29 ppm) agree excellently with the experimental values for the *trans* isomer, confirming the *trans* position of the aryl group and H-4-*endo*, which is in agreement with the X-Ray results (Figure 3). For the *cis* analogue, the two parameters (δ = 4.79 ppm, ring current effect +0.22 ppm) are strongly different.



Perspective view of **7c**.
Thermal ellipsoids have been drawn
at a probability level of 30%

Figure 3

When the same criterion was applied to **6a** and **8**, the opposite result was obtained: H-5 at 5.00–5.29 ppm proves the position of the aryl and H-4-*endo* as *cis*. For **9**, however, the position of the tolyl group could not be assigned with certainty because of the many ^{1}H signals in the NMR spectrum. For **5, 9** and **10**, the other data are in complete agreement with the structures given in Schemes 1 and 2.

3. EXPERIMENTAL

The IR spectra were determined in KBr discs on a Perkin Elmer Paragon 1000 PC FT-IR spectrophotometer. NMR spectra were recorded with an AVANCE DRX 500 (Bruker) spectrometer. Chemical shifts ($CDCl_3$ for **4, 5, 6a,b, 7c, 8-10**; DMSO-d_6 for **7a** and **7b**) (δ, ppm, $\delta_{TMS} = 0$ ppm) are given. The corresponding ^{1}H and ^{13}C chemical shifts and H,H coupling constants *J*/Hz are listed for the compounds in the EXPERIMENTAL. The 2D NMR spectra were acquired with standard Bruker software. Typical parameters were (*i*) gs-COSY-45: sweep width 2620 Hz, 1 k data points in F_2, 128 experiments in F_1 (20 scans, 4 dummy scans), relaxation delay 1.2 s; (*ii*) gs-HMQC: sweep width in F_1 10 kHz and in F_2 26*0 Hz, 1 k data points in F_2, 128 experiments in F_1 (8 scans, 2 dummy scans), relaxation delay 1.2 s, zero filling to 2 k data points in F_2 and 256 data points in F_1, filter function square sine-bell in both dimensions; (*iii*) gs-HMBC: sweep width in F_1 10 kHz and in F_2 2620 Hz, 1 k data points in F_2, 128 experiments in F_1 (40 scans, 2 dummy scans), relaxation delay 1.2 s, delay for evolution of long-range couplings 50 ms, zero filling, 1 k data points in F_2 and 256 data points in F_1, filter function shifted square sine-bell in both dimensions; (*iv*) NOESY: sweep width 2670 Hz, 1 k data points in F_2, 128 experiments in F_1 (40 scans, 4 dummy scans), relaxation delay ~5 times T_1, mixing time ~T1. The pulse widths (90^{o}) for all experiments were 12.5 μs (^{1}H), and 11.3 μs (^{13}C).

Quantum Chemical Calculations: The *ab initio* quantum-mechanical calculation on **7c** was performed on SGI Octane and SGI Origin 2000 work stations, using Gaussian 98.[21] Geometry optimization was carried

out by using HF/6-31G* without constraints.[22] The shielding constants were calculated with the GIAO method[23,24] at the same level of theory; since the GIAO approach is gauge-invariant, it can be applied for the calculation of NICS. The studied phenyl ring was placed in the centre of a grid of lattice points, ranging from –10Δ to +10Δ in all three dimensions (step width 0.5Δ), resulting in a cube of 68921 lattice points. The coordinates and shielding values of the lattice points around phenyl were transformed into SYBYL[25] contour files and the anisotropic effect visualized as iso-chemical-shift-surfaces (ICSS). In this way, it was possible to map the spatial extent, sign and scope of the corresponding anisotropic effect in **7c** at each fixed stereochemical position.[26]

X-Ray data collection and processing: Crystallographic data were collected at 173 K on a Nonius Kappa CCD area-detector diffractometer, using graphite monochromatized MoK_α ($\lambda = 0.71073$ Å). The data collection was performed by using φ and ω scans. The data were processed with DENZO-SMN v0.93.0.[27]

Crystal Data for **3b**: ($C_{15}H_{16}O_4$, $M_r = 260.28$), orthorhombic, $a = 5.7656(2)$, $b = 13.0113(4)$, $c = 16.7088(7)$ Å, $\alpha = \beta = \gamma = 90°$, $U = 1253.46(8)$ Å^3, $T = 173$ K, space group $P2_12_12_1$ (no. 19), $Z = 4$, $\mu(Mo–K_\alpha) = 0.100$ mm^{-1}, 1978 unique reflections, which were used in calculations. The final $wR(F^2)$ was 0.0889 (all data).

Crystal Data for **7c**: ($C_{18}H_{21}NO_3$, $M_r = 299.36$), triclinic, $a = 8.2783(2)$, $b = 10.05320(10)$, $c = 10.9091(2)$ Å, $\alpha = 64.3510(10)$, $\beta = 71.3170(10)$, $\gamma = 71.3170(10)°$, $U = 746.56(2)$ Å^3, $T = 173$ K, space group *P1* (no. 2), $Z = 2$, $\mu(Mo–K_\alpha) = 0.090$ mm^{-1}, 2610 unique ($R_{int} = 0.017$), which were used in calculations. The final $wR(F^2)$ was 0.0895 (all data).

The structures were solved by direct methods with SIR92,[28] and full-matrix least-squares refinements on F^2 were performed with SHELXL-97.[29] For both, all heavy atoms were refined anisotropically. The phenyl and methyl CH hydrogen atoms were included at fixed distances, with fixed displacement parameters from their host atoms. The remaining hydrogen atoms were refined isotropically. Figures were drawn with Ortep-3 for Windows.[30]

CCDC 209077 & 209078 contain the supplementary crystallographic data for this paper.

3-*exo*-*p*-Toluoyl-7-oxabicyclo[2.2.1]heptane-2-*exo*-carboxylic acid (3a)

8.41 g (0.05 mol) of **2** was added to a stirred suspension of 16.66 g (0.125 mol) of $AlCl_3$ in dry CH_2Cl_2 (50 mL), and a solution of 4.61 g (0.05 mol) of toluene in CH_2Cl_2 (10 mL) was then added dropwise during 30 min at rt; stirring was continued for 8 h. After standing overnight, the mixture was poured onto ice (200 g) and 36% HCl (20 mL), and extracted with $CHCl_3$ (2 × 50 mL). The extract was washed with water, dried (Na_2SO_4) and evaporated. The residue was taken up in $CHCl_3$ (20 mL), and *n*-hexane (20 mL) was added to the solution; the solid was filtered off, and recrystallized. **3a**: IR (KBr): ν

[cm^{-1}] = 1728 (C=O), 1665 (C=O, ketone). H-MS: 260.1094 ($C_{15}H_{16}O_4$), MS: m/z (%) 260 (5), 137 (12), 119 (100), 96 (14), 91 (38), 68 (38), 39 (12). Physical and analytical data on **3a** are listed in Table 1.

Table 1. Physical and analytical data on compounds (**3a-10**)

Com-pound	mp °C	Yield %	Formula	Analysis Found %			Calcd %		
				C	H	N	C	H	N
3a	194-196[a]	58	$C_{15}H_{16}O_4$	69.19	6.30		69.34	6.18	
3b	218-220[b]	17	$C_{15}H_{16}O_4$	69.20	6.10		69.32	6.24	
4	142-144[c]	83	$C_{15}H_{16}O_4$	69.02	6.35		69.28	6.15	
5	249-251[e]	65	$C_{15}H_{16}N_2O_2$	70.17	6.29	10.67	70.48	6.35	10.82
6a	137-138[d]	51	$C_{17}H_{20}N_2O_2$	71.71	7.00	9.95	71.85	7.15	9.75
6b	126-128[f]	39	$C_{19}H_{24}N_2O_2$	73.25	7.64	8.77	73.01	7.75	8.90
7a	192-194[d]	49	$C_{17}H_{19}NO_3$	71.46	6.71	4.98	71.68	6.82	4.87
7b	179-180[d]	50	$C_{18}H_{21}NO_3$	72.02	7.27	4.58	72.10	7.09	4.72
7c	172-173.5[d]	54	$C_{18}H_{21}NO_3$	72.12	7.27	4.70	72.25	7.12	4.60
8	247-249[d]	58	$C_{21}H_{20}N_2O_2$	75.98	6.27	8.45	75.78	6.15	8.32
9	221-223[g]	38	$C_{23}H_{25}N_3O_2$	73.54	6.75	11.29	73.68	6.60	11.05
10	231-233[b]	42	$C_{18}H_{17}N_3O_2$	70.28	5.48	13.50	70.49	5.62	13.73

Crystallization solvent: [a]$CHCl_3$–*n*-hexane; [b]EtOAc–EtOH; [c]Et_2O; [d]*i*-Pr_2O; [e]EtOH; [f]Et_2O–*n*-hexane; [g]EtOAc.

***diexo*-1-Hydroxy-1-*p*-tolylhexahydro-4,7-epoxybenzofuran-3-one (3b)**

2.60 g (0.01 mol) of **3a** was dissolved in a mixture of EtOAc–EtOH (9 : 1, 10 mL). After standing for a week at rt, the crystals that had separated out were filtered off. **3b**: IR (KBr): ν [cm^{-1}] = 3317 (OH), 1765 (C=O, lactone). H-MS: 260.108 ($C_{15}H_{16}O_4$), MS: m/z (%) 260 (41), 243 (81), 171 (12), 137 (12), 124 (19), 119 (100), 91 (29), 68 (17).

3-*endo*-*p*-Toluoyl-7-oxabicyclo[2.2.1]heptane-2-*exo*-carboxylic acid (4)

A mixture of oxocarboxylic acid (**3a**) (1.30 g, 5 mmol) in toluene (10 mL) and 2 drops of Et_3N was refluxed for 3 h. After cooling, the solid that had separated out was recrystallized. ^{1}H-NMR: 1.8 (H-1-*exo*), 1.7 (H-1-*endo*), 1.5 (H-2-*exo*), 1.4 (H-2-*endo*), 4.95 (H-3), 4.4 (H-4), 3.5 (H-5), 5.0 (H-6), 7.9 (H-10), 7.3 (H-11), 2,4 (H-13). ^{13}C-NMR: 29.3 (C-1), 25.8 (C-2), 79.4 (C-3), 55.6 (C-4), 50.0 (C-5), 81.3 (C-6), 179.1 (C-7), 196.2 (C-8), 134.4 (C-9), 129.1 (C-10), 130.1 (C-11), 145.2 (C-12), 22.1 (C-13). H-MS: 260.1093 ($C_{15}H_{16}O_4$), MS: m/z (%) 260 (6), 231 (4), 215 (3), 192 (81), 187 (13), 171 (35), 158 (12), 147 (7), 119 (100), 91 (31), 65 (7), 39 (3).

5,8-Epoxy-4-*p*-tolyl-4a,5,6,7,8,8a-hexahydro-2*H*-phthalazin-1-one (5)

A solution of **3a** (1.30 g, 5 mmol) and hydrazine hydrate (99%, 0.50 g, 0.01 mol) in EtOH (10 mL) was refluxed for 4 h, and then concentrated to half-volume. After standing at rt for 3 h, the product (**5**) was filtered off by suction. Recrystallization yielded colourless crystals. ^{1}H-NMR: 1.9-1.8 (4H, H-1, H-2),

4.7 (H-3), 3.4 (H-4), 3.0 (H-5), 5.1 (H-6), 7.6 (H-10), 7.2 (H-11), 2.4 (H-13), 8.52 (N*H*). ^{13}C-NMR: 29.6 (C-1), 30.1 (C-2), 83.7 (C-3), 45.4 (C-4), 47.6 (C-5), 83.2 (C-6), 164.6 (C-7), 147.0 (C-8), 132.9 (C-9), 126.3 (C-10), 129.9 (C-11), 140.4 (C-12), 22.2 (C-13). H-MS: 256.1221 ($C_{15}H_{16}N_2O_2$), MS: m/z (%) 256 (11), 200 (4), 187 (100), 171 (2), 155 (1), 141 (2), 128 (2), 115 (3), 91 (3), 77 (1).

6,9-Epoxy-9b-*p*-tolyl-2,3,5a,6,7,8,9,9a-octahydroimidazo[2,3-*a*]isoindol-5-one (6a), 8,11,epoxy-10b-*p*-tolyl-2,3,4,5,7a,8,9,10,11,11a-decahydro[1,3]diazepino[2,3-*a*]isoindol-7-one (6b), 6,9-epoxy-9b-*p*-tolyl-2,3,5a,6,7,8,9,9a-octahydro[2,3-*a*]isoindol-5-one (7a), 6,9-epoxy-2-methyl-9b-*p*-tolyl-2,3,5a,6,7,8,9,9a-octahydrooxazolo[2,3-*a*]isoindol-5-one (7b), 7,10-epoxy-10b-*p*-tolyl-2,3,6a,7,8,9,10,10a-octahydro[1,3]oxazino[2,3-*a*]isoindol-6-one (7c), 6,9-epoxy-9b-*p*-tolyl-5a,6,7,8,9,9a-hexahydrobenzimido[2,3-*a*]isoindol-5-one (8)

A mixture of **3a** (1.30 g, 5 mmol), a bicyclic reagent (ethylenediamine 0.45 g, 1,4-diaminobutane 0.66 g, ethanolamine 0.46 g, 1-amino-2-propanol 0.56 g, 1-amino-3-propanol 0.56 g, or *o*-phenylenediamine 0.81 g, 7.5 mmol) and PTSA (0.05 g) in chlorobenzene (10 mL) was refluxed for 10 h. After evaporation, the residue was dissolved in $CHCl_3$ (10 mL), transferred to an Al_2O_3 column (ACROS, basic, 50-200 μ) and eluted with *n*-hexane–EtOAc (1 : 1) for **6a, 6b** and **8**, or with *n*-hexane–EtOAc (2 : 1) for **7a, 7b** and **7c**. Physical and analytical data are collected in Table 1.

6a: ^{1}H-NMR: 1.7 (2H, H-1-*exo*, H-2-*exo*), 1.4 (H-1-*endo*), 1.25 (H-2-*endo*), 4.9 (H-3), 2.3 (H-4), 3.0 (H-5), 4.8 (H-6), 7.3 (H-10), 7.1 (H-11), 2.3 (H-13), 2.9 (2H, N(H)CH_2), 3.2 (2H, NCH_2). ^{13}C-NMR: 28.8 (C-1), 28.6 (C-2), 78.0 (C-3), 52.0 (C-4), 56.4 (C-5), 78.8 (C-6), 177.7 (C-7), 89.6 (C-8), 141.3 (C-9), 125.5 (C-10), 129.8 (C-11), 137.9 (C-12), 21.4 (C-13), 42.0 (NH*C*), 46.2 (N*C*). H-MS: 284.1492 ($C_{17}H_{20}N_2O_2$), MS: m/z (%) 284 (60), 269 (7), 254 (26), 240 (15), 210 (6), 193 (24), 184 (3), 170 (4), 159 (100), 131 (16), 118 (4), 105 (3), 91 (4), 77 (1), 65 (2), 41 (2).

6b: ^{1}H-NMR: 1.7 - 1.3 (4H, H-1, H-2), 3.7 (H-3), 2.4 (H-4), 2.8 (H-5), 4.8 (H-6), 7.0 (H-10), 7.5 (H-10a), 7.1 (H-11), 7.2 (H-11a), 2.3 (H-13), 3.0 and 2.4 (NHCH_2), 1.2 and 1.8 (CH_2), 1.5 and 1.8 (CH_2), 2.6 and 3.9 (NCH_2). ^{13}C-NMR: 29.6 (C-1), 28.2 (C-2), 79.8 (C-3), 56.2 (C-4), 53.6 (C-5), 78.1 (C-6), 175.1 (C-7), 86.1 (C-8), 138.7 (C-9), 127.0 (C-10), 127.2 (C-10a), 129.0 (C-11), 129.8 (C-11a), 138.2 (C-12), 21.4 (C-13), 42.6 (NH*C*), 33.0 (NHC*C*), 24.8 (NC*C*), 41.2 (N*C*). H-MS: 312.1812 ($C_{19}H_{24}N_2O_2$), MS: m/z (%) 312 (50), 282 (8), 268 (19), 254 (23), 240 (14), 221 (100), 198 (5), 187 (54), 170 (5), 131 (9), 118 (6), 105 (2), 91 (4), 70 (23), 68 (2), 41 (2).

7a: ^{1}H-NMR: 1.5 (2H, H-1), 1.4 (2H, H-2), 3.8 (H-3), 2.7 (H-4), 2.9 (H-5), 4.6 (H-6), 7.2 (H-10), 7.4 (H-10a), 7.3 (2H, H-11), 2.3 (H-13), 3.4 (OCH_2), 2.8 (NCH_2). ^{13}C-NMR: 28.5 (C-1), 27.3 (C-2), 77.6 (C-3), 50.7 (C-4), 53.6 (C-5), 77.7 (C-6), 180.9 (C-7), 103.0 (C-8), 134.5 (C-9), 128.5 (C-10), 126.7 (C-10a), 129.5 (C-11), 126.0 (C-11a), 137.7 (C-12), 20.8 (C-13), 62.8 (O*C*), 42.9 (N*C*). H-MS: 285.1351

($C_{17}H_{19}NO_3$), MS: m/z (%) 285 (77), 270 (17), 254 (100), 240 (57), 210 (9), 194 (12), 170 (4), 162 (31), 160 (25), 131 (14), 119 (12), 105 (5), 91 (10), 77 (2), 68 (5), 41 (2), 39 (2).

7b: ^{1}H-NMR: 1.5 (2H, H-1), 1.4 (2H, H-2), 3.6 (H-3), 2.7 (H-4), 2.9 (H-5), 4.6 (H-6), 7.1 (H-10), 7.4 (H-10a), 7.3 (2H, H-11), 2.3 (H-13), 3.5 (OC*H*), 1.1 (OCCH_3), 3.0 (NCH_2). ^{13}C-NMR: 28.5 (C-1), 27.3 (C-2), 77.6 (C-3), 51.0 (C-4), 53.5 (C-5), 77.7 (C-6), 180.9 (C-7), 103.3 (C-8), 135.0 (C-9), 128.4 (C-10), 126.4 (C-10a), 129.5 (C-11), 126.1 (C-11a), 137.6 (C-12), 20.8 (C-13), 71.1 (O*C*), 20.5 (O*C*CH_3), 49.9 (N*C*). H-MS: 299.1499 ($C_{18}H_{21}NO_3$), MS: m/z (%) 299 (66), 284 (29), 254 (100), 240 (56), 208 (9).

7c: ^{1}H-NMR: 1.7 (H-1-*exo*), 1.45 (H-1-*endo*), 1.55 (H-2-*exo*), 1.3 (H-2-*endo*), 2.4* (H-4), 2.95* (H-5) (*interchangeable data), 4.8 (H-6), 7.4 (H-10), 7.1 (H-10a), 7.2 (H-11), 7.3 (H-11a), 2.3 (H-13), 3.8 (OCH_2), 1.9 (CH_2), 4.1 (NCH_2). ^{13}C-NMR: 29.4 (C-1), 28.4 (C-2), 78.8 (C-3), 54.9* (C-4), 52.6* (C-5), 78.4 (C-6), 175.5 (C-7), 96.8 (C-8), 133.9 (C-9), 127.0 (C-10), 129,1 (C-10a), 129.7 (C-11), 130,2 (C-11a), 138.6 (C-12), 21.5 (C-13), 63,0 (O*C*), 25,7 (OC*C*), 37.5 (N*C*). H-MS: 299.1529 ($C_{18}H_{21}NO_3$), MS: m/z (%) 299 (51), 268 (42), 254 (100), 224 (5), 208 (82), 174 (11), 141 (1), 119 (13), 105 (2), 91 (7), 68 (2), 65 (2), 41 (2), 39 (1).

8: ^{1}H-NMR: 1.8 (H-1-*exo*), 1.5 (H-1-*endo*), 1.8 (H-2-*exo*), 1.5 (H-2-*endo*), 5.3 (H-3), 2.7 (H-4), 3.1 (H-5), 4.9 (H-6), 7.3 (H-10), 7.5 (H-11), 2.3 (H-13), 6.7 (1H), 6.8 (1H), 6.9 (1H), 7.5 (1H), 4.5 (N*H*). ^{13}C-NMR: 28.2 (C-1), 29.5 (C-2), 78.7 (C-3), 53.5 (C-4), 57.4 (C-5), 79.4 (C-6), 176.1 (C-7), 89.5 (C-8), 143.9 (C-9), 123.9 (C-10), 116.1 (C-11), 138.4 (C-12), 21.4 (C-13), 138,4 (s, 1C), 142,7 (s, 1C), 111.9 (d, 1C), 126.1 (d, 1C), 120.9 (d, 1C), 116.1 (d, 1C). H-MS: 332.1695 ($C_{21}H_{20}N_2O_2$), MS: m/z (%) 332 (79), 303 (2), 241 (64), 208 (100), 124 (3), 91 (2), 68 (2).

1,4-Epoxy-9,12-methano-5-*p*-tolyl-8*H*-1,2,3,4,4a,8a,9,10,11,12,12a,13b-dodecahydrophthalazino[1,2-*b*]quinazolin-8-one (9), 8,11-epoxy-7-*p*-tolyl-7a,8,9,10,11,11a-hexahydro-4*H*-pyrimido[2,1-*a*]phthalazin-4-one (10)

A mixture of **3a** (2.60 g, 0.01 mol) and *diexo*-3-aminobicyclo[2.2.1]heptane-2-carbohydrazide (1.69 g, 0.01 mol) or *diendo*-3-aminobicyclo[2.2.1]hept-5-ene-2-carbohydrazide (1.67 g, 0.01 mol) in toluene (30 mL) was refluxed for 16 h, a Dean-Stark water separator being applied. After evaporation, the residue was dissolved in $CHCl_3$ (20 mL). The solution containing **9** was transferred onto a silica gel column (ACROS, 0.035-0.07 mm) and eluted with EtOAc; the solution of **10** was transferred onto an Al_2O_3 column (ACROS, basic, 50-200 μ) and eluted with EtOAc–*n*-hexane (2 : 1). Both of the residues were crystallized.

9: ^{1}H-NMR: 1.8 (H-1), 1.4 + 1.7 (H-2-*exo*, H-2-*endo*)* (the assignments of *exo* and *endo* may be reversed), 4.55 (H-3), 3.16 (H-4), 3.0 (H-5), 4.9 (H-6), 7.65 (H-10), 7.15 (H-11), 2.3 (H-13), 2.75 (H-15), 3.75 (H-16), 2.45 (H-17), 1.2 + 1.4 (H-18-*exo*, H-18-*endo*),* 1.7 + 1.5 (H-19-*exo*, H-19-*endo*),* 2.7 (H-20), 1.2 + 1.4 (H-21). ^{13}C-NMR: 28.9 (C-1), 30.3 (C-2), 83.4 (C-3), 42.8 (C-4), 46.7 (C-5), 86.7 (C-6), 144.4

(C-7), 149.6 (C-8), 133.2 (C-9), 127.0 (C-10), 129.8 (C-11), 140.8 (C-12), 21.7 (C-13), 165.7 (C-14), 50.1 (C-15), 62.7 (C-16), 46.4 (C-17), 26.5 (C-18), 30.0 (C-19), 44.5 (C-20), 34.7 (C-21). H-MS: 375.1965 ($C_{23}H_{25}N_3O_2$), MS: m/z (%) 375 (100), 346 (24), 332 (95), 306 (34), 278 (5), 264 (6), 238 (5), 212 (4), 208 (4), 169 (2), 129 (1), 121 (3), 115 (2), 91 (2).

10: ^{1}H-NMR: 1.6-2.0 (m, 4H, H-1, H-2), 4.7 (H-3), 3.4 (H-4), 3.4 (H-5), 5.1 (H-6), 7.7 (H-10), 7.2 (H-11), 2.3 (H-13), 6.4 (COC*H*), 7.71 (NC*H*). ^{13}C-NMR: 24.3 (C-1), 30.3 (C-2), 84.0 (C-3), 43.4 (C-4), 46.8 (C-5), 86.4 (C-6), 151.7 (C-7), 155.5 (C-8), 132.1 (C-9), 127.7 (C-10), 130.0 (C-11), 142.3 (C-12), 21.9 (C-13), 148.5 (N*C*=O), 115.8 (O=C*C*), 151.5 (N*C*). H-MS: 307.1305 ($C_{18}H_{17}N_3O_2$), MS: m/z (%) 307 (37), 278 (9), 264 (100), 250 (10), 238 (74), 209 (6), 169 (11), 153 (6), 134 (5), 128 (9), 115 (16), 106 (4), 91 (20), 80 (7), 70 (9), 65 (12), 53 (8), 41 (12), 39 (10).

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