Acta Chemica Scandinavica, 1998: 52: 322–327
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ACTA
CHEMICA SCANDINAVICA
ISSN 0904–213X

Synthesis and Structure of Methanobenzocyclooctene Derivatives†

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Miklós, F., Csende, F., Stájer, G., Sohár, P., Sillanpää, R., Bernáth, G. and Szúnyog, J., 1998. Synthesis and Structure of Methanobenzocyclooctene Derivatives. – Acta Chem. Scand. 52: 322–327. © Acta Chemica Scandinavica 1998.

10-Oxo-5,9-methanobenzocyclooctene-8-carboxylic acid **4a** was prepared by the intramolecular cyclization of 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylic acid **1a** in concentrated H_2SO_4 or in the reaction of 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylic anhydride **2** in 80% H_2SO_4. To improve the yield, the esters **3a,b** were cyclized to the methanocyclooctene isomers **5a,b**, in a 1:5 ratio from **3a**, and in a 5:4 mixture (54%) from **3b** at elevated temperature. After separation, **5a** was hydrolysed, the keto group of **4a** was reduced by the Wolff–Kishner method and the resulting *cis* and *trans* methylene-bridged benzocyclooctenes **6a,b** (1:2) were separated. From **4a** with hydrazine, the tetracyclic pyridazinone derivative **7** was obtained. The structures were determined by ^1H and ^{13}C NMR methods and for **4a** also by X-ray crystallography.

In our earlier studies on fused-skeleton saturated and partially saturated 1,3-heterocycles, we studied the reactions of cyclic β-oxo carboxylic acids with alicyclic 1,3-amino alcohols in which one of the functional groups was attached directly, and the other through a methylene group to carbocycles such as cyclohexane, cyclohexene, norbornane or norbornene.[1–4] In these cyclizations, tetracyclic and pentacyclic hetero compounds were formed, and isomerization of the starting stereohomogeneous *cis* and *trans* amino alcohols also often occurred. Consequently, structure elucidation of the fairly complex tetracyclic or pentacyclic systems, and determination of the configuration and conformation, was always a challenging task; a comparative study of closely related ring systems and the *cis*- and *trans*-fused isomers added to the importance. The new compounds were synthesized with pharmacological aims.

For the synthesis of fused-skeleton isoindolones, *cis*- or *trans*-2-aroyl-1-cyclohexanecarboxylic acids were used as starting materials in our earlier studies. In the present paper, *cis*-4-cyclohexene-1,2-dicarboxylic anhydride was applied; through the addition of benzene to the double bond,[5] this furnished 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylic acid **1a** with a phenyl equatorial[3] to the neighbouring carboxy group. The 4-phenyl substituent on cyclohexane-1,2-dicarboxylic acid was thought might provide a good opportunity to construct highly condensed systems by intramolecular acylation of the phenyl substituent with the 2-carboxy group. These systems containing two functional groups are suitable for the preparation of heterocycles and they provide good starting molecules for the production of new pharmacologically active derivatives as target compounds.

Results

When heated in concentrated H_2SO_4, *trans*-4-phenylcyclohexane-*cis*-1,2-dicarboxylic acid (**1a**) or in 80% H_2SO_4, the anhydride **2** yielded 10-oxo-5,6,7,8,9,10-hexahydro-5,9-methanobenzocyclooctene-8-carboxylic acid (**4a**; yield 13% and 15%, respectively) by intramolecular cyclization.

Similar cyclization via $AlCl_3$-catalysed intramolecular Friedel–Crafts acylation provides only a moderate yield (14–21%),[6] in spite of the absence of strain in the bicyclononanone ring system.[7] Other preparations,[8,9] e.g., from benzylcyclohexanone with MeLi,[10] from unsaturated enol silyl esters with ceric ammonium nitrates,[11,12] from alkenes by $MeSO_3H$ cyclization[13] and by carbo-

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† Saturated Heterocycles, Part 255. Part 254: Bernáth, G., Miklós, F., Stájer, G., Sohár, P., Böcskei, Zs. and Menyhárd, D. *J. Heterocycl. Chem. In press.*

cationic cyclization of unsaturated bromo imines[14] are also known.

To improve the yield of **4a**, we started from dimethyl 4-*trans*-phenylcyclohexane-*cis*-1,2-dicarboxylate (**3a**); cyclization with PPA at elevated temperature yielded a mixture of the isomeric esters **5a** and **5b** in a ratio of 1:5. In contrast, cyclization of dimethyl 4*t*-phenylcyclohexane-1*r*,2*t*-dicarboxylate (**3b**) gave the esters **5a** and **5b** in a 5:4 ratio (the yield of **5a,b** was 54%). Consequently, as a result of the transformation **3b** → **5a,b** with PPA, the 30% yield of **5a** (Table 3) isolated from the mixture **5a,b** by column chromatography proved to be enough to permit further reactions. We presume that in the cyclization the 2-carboxy groups which are axial in the ground state come close to the phenyl group by ring inversion and **3a** and **3b** partly isomerize to form the products **5a,b**. After separation of the isomers, the structures were established by NMR spectroscopy. The esters **5a,b** were hydrolysed and the acids **4a,b** were characterized by NMR and for **4a** also by X-ray analysis (Fig. 1). The oxo group was reduced by the Wolff–Kishner method to afford a mixture of *cis*- and *trans*-5,6,7,8,9,10-hexahydro-5,9-methanobenzocyclooctene-8-carboxylic acids (**6a,b**). With hydrazine, the oxo

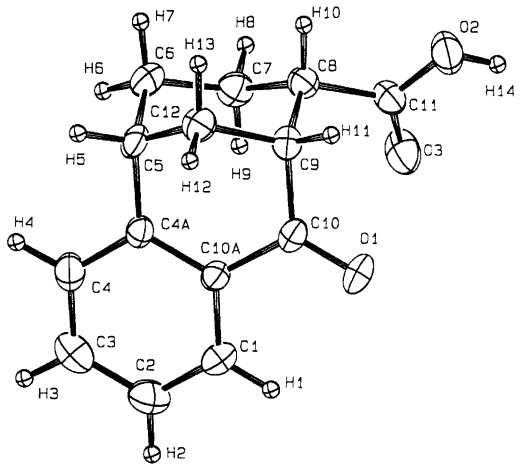


Fig. 1. X-Ray structure of compound **4a**.

Table 1. IR carbonyl frequencies in KBr[a] and ^{1}H NMR data[b] on compounds **4–7** in $CDCl_3$ solution[c] at 250 MHz.[d]

Compound	$\nu_{C=O}$ Posn. 8	$\nu_{C=O}$ Posn. 10	H-1 dd (1 H)	H-4 dd (1 H)	H-5,9[e] m (2 H)	H-ax Posn. 7	H-8 m (1 H)	H-eq[f] Posn. 11
4a	1713	1678	8.03	7.24	≈3.2	1.50[g]	2.79[h]	2.50[i]
4b	1696	1681	8.04	7.24	3.25	1.48[j]	2.94[k]	2.30[l]
5a	1728	1681	8.06	7.23	≈3.2	1.52[g]	2.73[h]	2.45[i]
5b	1729	1679	8.05	7.25	3.18	1.40[j]	2.85[k]	2.25[l]
6a	1712	—	≈7.1[m]	7.00	2.98[n]	1.35[g]	≈2.7[o]	2.00[l]
6b	1701	—	≈7.1[m]	7.00	2.98	1.45[j]	2.68[o]	≈2.0[p]
7	1671	—	7.80	7.20	≈3.1	1.35[g]	2.55[h]	2.00[l]

[a] In cm^{-1}. [b] Chemical shifts in δ, $\delta_{TMS}=0$ ppm, coupling constants in Hz. [c] **4a** was also measured in DMSO-d_6 solution. [d] Assignments were proved by DR (**4a**) and DNOE (**6a,b**) measurements. Further signals, ^{1}H NMR: CH_3 (s, 3 H): 3.72 (**5a**), 3.77 (**5b**); CH_2 (posn. 6, 7eq, 11ax), 4 × m (4 × 1 H) in the interval 1.7–2.2 ppm, partly overlapped. Separated signals: H-6ax: 1.90[j] (**4a**, **5a**), 2.18[j] (**4b**), H-6eq: 1.85[l] (**4a**), 1.65[l] (**4b**), 1.80[l] (**5a**), 1.60[l] (**5b**), 1.55[l] (**6b**), H-7eq: 1.75[l] (**4a**, **5a**), 2.05[l] (**4b**), 1.98[l] (**5b**), H-11ax: 2.05[h] (**4a**, **5a**), 2.22[h] (**4b**), 1.85[h] (**6a**); CH_2 (posn. 10): 2.78 d (split by 18.4) and 2.98[n] (**6a**), 2.68[o] and 3.27 dd (split by 18.0 and 7.5) for **6b**; H-2,3, 2 × dt (2 × 1 H): 7.30 and 7.50 (**4a**, **5a,b**), 7.38 and 7.55 (**4b**), coalesced at ≈7.1 (**6a,b**) and 7.3 (**7**); NH, (br s, 1 H): 8.65 (**7**); H-9 (≈s, 1 H): 3.00 (for **4a** in DMSO-d_6); IR, ν_{OH}: 3300–2200 (**4a,b**, **6a,b**); ν_{NH}: 3185 (**7**). [e] Overlapping signals, except for **6a,b**, where the H-9 signal at about 2.7 ppm is coalesced with the H-8 m (**6a**) and the upfield m of CH_2 (posn. 10) group (**6b**). [f] To ring *C* (*S-cis* to the condensed aromatic ring). [g] Quartet split by ca. 13.5 with further doublet split by ca. 4.5. [h] Doublet (split by 13.2 ± 0.2) with further triplet split by ca. 4 (for H-8) or 2.5 (H-11ax). [i] Quartet (split by ca. 13) with further quartet split by 2.5. [j] Triple triplet split by ca. 13.5 (H-6ax) or 14.5 (H-7ax) and 4. [k] Singlet-like signal with coalesced fine structure. [l] Doublet-like signal with coalesced further fine structure, split by 14 ± 0.5. [m] In overlap with the H-2,3 signal. [n,o] Overlapping signals. [p] In overlap with the H-6ax signal.

Table 2. ^{13}C NMR chemical shifts[a] of compounds **4–7** in $CDCl_3$ solution at 63 MHz.[b]

Compound	C-1	C-2	C-3	C-4	C-4a	C-5	C-6	C-7	C-8[c]	C=O	C-10[c]	C-9[c]	C-11	C-10a[c]
4a	125.4	126.8	134.2	128.5	147.1	33.6	29.8	19.6	44.4	174.1	198.1	45.0	33.2	133.7
4b	126.7[d]	127.0[d]	134.4	128.2[d]	147.2	34.5	27.6	19.1	41.9	179.6	200.3	43.8	29.9	133.3
5a[e]	126.9	126.5	134.1	128.0	146.8	34.3	30.3	19.7	45.3	173.4	198.5	45.4	33.8	134.0
5b[e]	126.0	126.4	133.7	127.7	146.7	34.0	27.1	18.7	41.3	173.1	199.4	43.6	29.3	132.8
6a	128.0[f]	125.7	125.4	128.0[f]	140.5	33.6	33.2	19.2	47.8	181.2	30.7	29.5	31.7	137.0
6b	127.9	125.7	125.5	128.2	140.6	33.7	30.2	18.8	46.5	181.3	35.3	28.8	27.8	136.8
7	123.5	127.4[d]	129.5	127.9[d]	143.4	32.2	28.9[f]	18.3	35.0	174.9	157.6	39.0	28.9[f]	133.3

[a] $\delta_{TMS}=0$ ppm. [b] Assignments were confirmed by 2D-HSC (except for **4b** and **7**) and DEPT measurements. [c] For easier comparison of spectroscopically analogous data, the numbering of **4** and **5** is used also for **6** and **7** here and in the text. The IUPAC numbering is given in the Experimental part. [d] Interchangeable assignments. [e] OCH_3: 51.8 (**5a**), 51.5 (**5b**). [f] Two overlapping lines.

carboxylic acid **4a** was cyclized to the tetracyclic methanobenzocycloocta[9,8-*c*,*d*]pyridazinone **7**.

Structure. The characteristic IR, ^{1}H and ^{13}C NMR data are listed in Tables 1 and 2. For the isomeric pairs **4a,b** and **5a,b**, establishment of the stereo structure is complicated by the flexibility of ring *C* resulting in two relatively stable (chair and boat) conformations. Hence, both the C-8 configuration and the conformation have to be determined.

Owing to the strong steric hindrance between the α-axial COOR group and the skeleton (no sign of which appears in the spectra), the presumption of a *cis* H-8,H-9 configuration (5*R**,8*S**,9*R**) allows no boat conformation of ring *C* (Scheme 1, **4a***i*). For a chair conformation and a *cis* configuration (Scheme 1, **4a***ii*), the axial H-8 is in a *trans*-diaxial position with one of the neighbouring H-7 atoms, and the correspondingly large coupling[15] appears in the ^{1}H NMR spectra of one each of the acid and ester isomers; for **4a** and **5a**, the H-8 signal is a triplet of doublets split by 13.3, 4.1 and 4.1 Hz. (For a boat conformation of ring *C*, the equatorial H-8 would not display as large coupling as 13.3 Hz.)

As the H-8 multiplet of **4b** and **5b** does not exhibit a large splitting, the chair conformation of ring *C* is also preferred for the *trans* isomers (5*R**,8*R**,9*R** configuration); hence, the COOR group is axial and the equatorial H-8 has no diaxial (i.e., large vicinal) coupling (Scheme 1). Accordingly, for *trans* **4b** and **5b**, the ^{13}C NMR spectra indicate a sterically more unfavourable structure: the sum of the chemical shifts of the carbons in ring *C* is less[16a] (by 8.8 and 14.8 ppm) than that for the isomers **4a** and **5a**. If the simultaneous alteration of the C-8 configuration and *C*-ring conformation for the *trans* isomers is assumed, no essential difference in steric hindrance would be observable in comparison with the *cis* compounds, because the COOR group is equatorial in both isomers.

Further proof of the tentative structures is the field effect[16b] (i.e., the upfield shift of the ^{13}C lines[17]), which indicates sterically unfavourable structures and which is higher for the C-6 and C-11 (and of course C-8) lines than for the other three carbons (C-5,7,9), because the first two carbons are positioned 1,3-diaxially to the 8-COOR group. For the *cis–trans* pairs of acids and esters, the sum of the shift differences for the C-6,8,11 lines amounts to 8.0 and 11.7 ppm, while the corresponding values for C-5,7,9 are only 0.8 and 3.1 ppm.

For **4a**, the X-ray determination (Fig. 1) revealed that the compound forms hydrogen-bonded monomers in the solid state. In the H-bond [O(2) ··· H(14) ··· O(3_I), $I = -x, 2-y, -z$], the O ··· O distance is 2.661(2) Å and the OH ··· O angle is linear 177(2)°. These are typical values for carboxylic acid dimers.

The spectral data on the reduced products **6a,b** confirm the above structures. For C-7 and C-11, the chemical shifts hardly differ from those measured for **4a,b** and **5a,b**. In the event of a boat conformation, the hindrance between the axial H-7 and H-11 would cause a strong steric effect, i.e., significant upfield shifts of the C-7 and C-11 lines. On the basis of the summed carbon shifts for ring *C* (the difference is 9.2 ppm), the assignments of the *cis* (5*R**,8*S**,9*S**) and *trans* (5*R**,8*R**,9*S**) H-8,H-9 configurations to the two isomers are unambiguous.

As stated above, for the isomeric pairs **4a,b** and **5a,b**, the shifts of C-6, C-8 and C-11 differ significantly due to the strong steric hindrance between the axial 8-COOR group and H-6_{ax} and H-11_{ax} in the *trans* isomers. For **6a,b**, only the shift difference for C-6 and C-11 is significant; that for C-8 is significantly smaller (Δδ C-8 = 1.3 ppm). The explanation lies in the strong steric hindrance between the *endo* 10-methylene hydrogen and the equatorial 8-COOH group of the *cis* isomer, and therefore the C-8 line is also shifted upfield for the *cis* isomer.

For steric reasons, the *cis* H-8,H-9 (5*R**,8*S**,9*R**) configuration is retained in the tetracyclic **7**, while for the starting **4a**, a change in the configuration on ring closure is not expected. The splittings of H-8 (13, 4 and 4 Hz) suggest the chair form of ring *C*, i.e., the conformation remains; the ≈13 Hz split confirms diaxial coupling (Scheme 1), and such an interaction is impossible in the boat form (H-8 would not be equatorial).

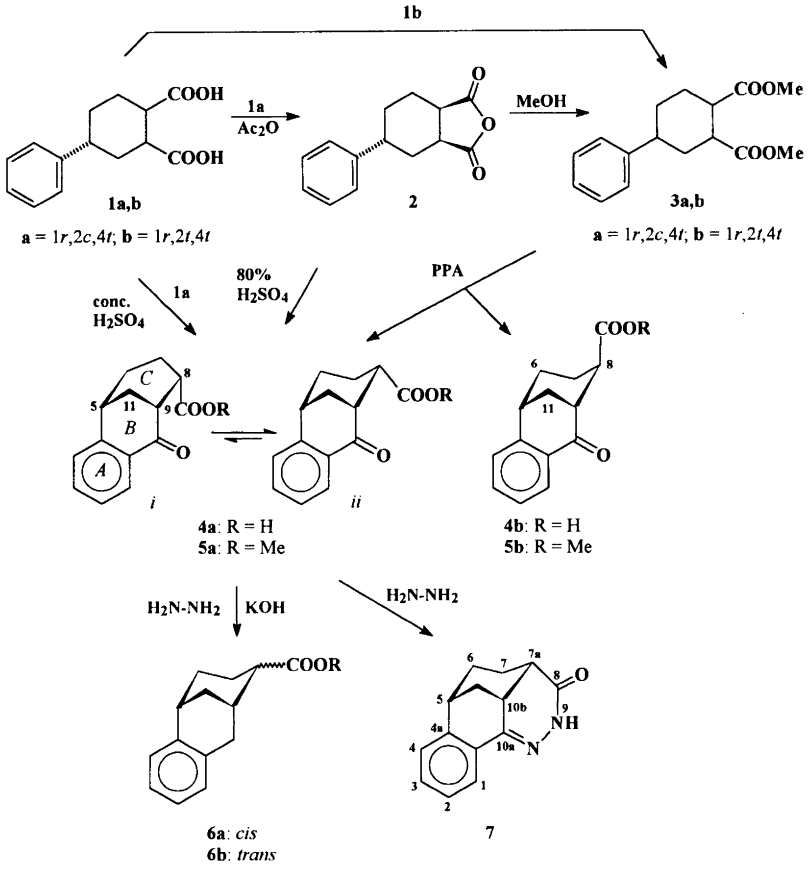
Conclusions

To summarize, the intramolecular cyclization of **3a** with PPA yielded the isomers **5a** and **5b**, which differ in the configuration of C-8; for **5a**, H-5, H-8 and H-9 lie on the same side of ring *C*, while in **5b**, H-5 and H-9 are on the same side and opposite to the hydrogen geminal to the carboxy group. On reduction of the acid **4a**, the isomers **6a** (all-*cis*) and **6b** (5*r*H,8*t*H,9*c*H) are formed in a 1:2 ratio; the epimerization probably takes place via enolization of the 8-CO (carboxy) group.

5a can be prepared from the *trans* ester **3b** more advantageously than from the *cis* ester **3a**, and its 30% yield allows its use as a starting molecule for the synthesis of highly condensed systems. Hence, intermolecular acylation with PPA at an elevated temperature is an appropriate method of obtaining the methanobenzocyclooctene system.

Experimental

IR spectra were run for samples in KBr discs on a vacuum optic Bruker IFS-113v FT spectrometer equipped with an Aspect 2000 computer. ^{1}H and ^{13}C NMR spectra were recorded for $CDCl_3$ solutions in 5 mm tubes at room temperature, on a Bruker WM-250 FT-spectrometer controlled by an Aspect 2000 computer at 250 (^{1}H) and 63 (^{13}C) MHz, respectively, using the deuterium signal of the solvent as the lock and Me_4Si as an internal standard. For DNOE measurements,[16c,18] the standard Bruker microprogram DNOEMULT.AU to generate NOE was used. 2D-HSC spectra[19] were obtained by using the standard Bruker pulse program



Scheme 1.

XHCORRD.AU. DEPT spectra[20] were run in a standard way,[21] using only the $\theta = 135°$ pulse to separate the CH/CH_3 and CH_2 lines phased up and down, respectively.

Crystal data for **4a**. Triclinic, space group $P\bar{1}$ (No. 2), $a = 8.526(2)$, $b = 10.784(2)$, $c = 7.368(2)$ Å, $\alpha = 93.97(2)$, $\beta = 112.68(2)$, $\gamma = 67.53(1)$, $V = 575.2(3)$ Å^3, $Z = 2$, $D_c = 1.329$ g cm^3, μ(Mo Kα) = 0.87 cm^{-1}, $F(000) = 244$, $T = 294(1)$ K, colourless prisms, crystal dimensions $0.26 \times 0.34 \times 0.40$ mm.

Data collection and refinement. A Rigaku AFC5S diffractometer was used with graphite monochromated Mo Kα radiation ($\lambda = 0.710\,69$) in the ω–2θ scan mode with a ω scan rate of 8.0° min^{-1} and a scan width of $1.63 + 0.30 \tan\theta$. The weak reflections [$F < 10\sigma(F)$] were rescanned up to two times. The data obtained were corrected for Lorentz and polarization effects. A total of 2165 unique reflections were measured ($2\theta_{max} = 50°$ and $R_{int} = 0.011$). The structure was solved by direct methods[22] and difference Fourier syntheses.[23] Structural parameters were refined by a full-matrix least-squares refinement, non-hydrogen atoms with anisotropic, and non-aromatic hydrogen atoms with fixed isotropic temperature parameters (1.2 times B_{eq} of carrying atom). The aromatic hydrogens were kept in the calculated positions. In the final cycles, the 1531 data with $I > 2\sigma(I)$ yielded an R value of 0.043 ($R_w = 0.037$, sigma weights) for 184 parameters. The residual electron density was from 0.15 to 0.17 e Å^3.

All calculations were performed with TEXSAN-89 software,[24] using a VAXSTATION 3520 computer. The neutral atomic scattering and dispersion factors were those included in the program. Figures were drawn with ORTEP.[25] The final atomic positional coordinates, bond lengths and angles have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Rd., Cambridge, CB2 1EW, UK.

HPLC: ISCO system with two pumps, suitable for gradient elution. The Chem. Research control system and data processing program were used. For the semi-preparative separation, a 5 µm BST Si-100-S 10-RP-18 column (250 × 16 mm) was used; eluent: *n*-hexane–isopropyl alcohol (98 : 2 v/v%); flow rate: 8 ml min^{-1}; injected sample: 250 µl; 0.5 g dichloromethane–eluent (1 : 3) detection at 220 nm.

10-Oxo-5r,6,7,8c,9c,10-hexahydro-5,9-methanobenzocyclooctene-8-carboxylic acid (**4a**): *method A.* 4*t*-Phenylcyclohexane-1*r*,2*c*-dicarboxylic acid[5] (**1a**) (5.0 g, 0.02 mol) in concentrated H_2SO_4 (20 ml) was heated to 150 °C and kept at this temperature for 1 h. After being cooled, the mixture was poured onto ice and extracted

with CH_2Cl_2 (3 × 20 ml). The extract was washed with water and dried (Na_2SO_4). On evaporation, the residue crystallized from EtOAc, m.p. 210–215 °C, yield 0.60 g (13%). Analytical data: found C 73.2; H 6.1. Calc. for $C_{14}H_{14}O_3$: C 73.0; H 6.1%.

Method B. To H_2SO_4 (80%, 30 ml), 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylic anhydride (**2**) (5.0 g, 0.02 mol) was added in portions, with stirring. The mixture was kept at 80 °C for 16 h and, after being cooled, poured onto ice and then extracted with $CHCl_3$ (3 × 300 ml). The extract was washed with water (2 × 50 ml), dried (Na_2SO_4) and evaporated to dryness. The product (**4a**) was purified on a silica gel column (Acros 0.035–0.07 mm) eluting with *n*-hexane–EtOAc (2:1). On evaporation, the residue crystallized from EtOAc, yield 0.70 g (15%).

*Dimethyl 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylate* (**3a**) *and 4*t*-phenyl-1*r*,2*t*-dicarboxylate* (**3b**). A mixture of anhydride **2**[26] (4.6 g, 0.02 mol) or dimethyl 4*t*-phenylcyclohexane-1*r*,2*t*-dicarboxylate **1b** (5.0 g, 0.02 mol) and benzene (25 ml) in MeOH (45 ml) was refluxed with concentrated H_2SO_4 (0.23 ml) for 4 h, a Dean–Stark water separator being applied. After evaporation of the solvent, the residue was neutralized with Na_2CO_3 solution (5%) and extracted with Et_2O (3 × 25 ml). The Et_2O extract was washed with water (2 × 20 ml), dried (Na_2SO_4) and evaporated to dryness. The residue was loaded onto a silica gel column (Acros 0.035–0.07 mm) and eluted with *n*-hexane–EtOH (5:1). On evaporation, the yield was 4.30 g (78%) **3a**, n_D^{23}: 1.5176, or 4.73 g (86%) **3b**, n_D^{23}: 1.5162. The products were used for the further preparations without purification.

*Cyclization of dimethyl 4*t*-phenylcyclohexane-1*r*,2*c*-dicarboxylate* (**3a**) *to the isomeric methyl esters* (**5a** and **5b**). To PPA (28.0 g), **3a**[3] (2.76 g, 0.01 mol) was added dropwise at 110 °C with stirring. The mixture was heated at this temperature for 3 h, then cooled and poured onto crushed ice. The mixture was extracted with Et_2O (3 × 150 ml), and the combined extract was washed with water (2 × 200 ml), dried (Na_2SO_4) and evaporated to dryness. The residue was transferred onto a silica gel column (Acros 0.035–0.07 mm) and eluted initially with an *n*-hexane–EtOAc mixture (5:1). First **5b** was eluted [higher R_f, monitoring by TLC, Alufolien Kieselgel 60 F_{254} Merck, 0.2 mm, solvent: benzene–EtOH–petroleum ether (b.p. 40–60 °C) 4:1:3, development in iodine vapour] and **5a** (lower R_f) was then eluted with an *n*-hexane–EtOAc mixture 4:1 mixture. On evaporation of the solvents and crystallization, from EtOAc–Et_2O, m.p. 122–123 °C, yield 0.77 g (31.5%) (**5b**) and from EtOAc, m.p. 105–107 °C, yield 0.15 g (6%) (**5a**) were obtained. Analytical data: found C 73.6; H 6.55 (**5b**) and C 73.85; H 6.8 (**5a**). Calc. for $C_{15}H_{16}O_3$: C 73.75; H 6.6%.

*Cyclization of dimethyl 4*t*-phenylcyclohexane-1*r*,2*t*-dicarboxylate* (**3b**) *to the isomeric 5,6,7,8,9,10-hexahydro-5,9-methanocyclooctene derivatives* (**5a,b**). The reaction was performed with **3b** (2.76 g, 0.01 mol) according to the cyclization of **3a** to **5a,b** in PPA, but at 120 °C. After chromatographic purification (silica gel column, Acros 0.035–0.07 mm; *n*-hexane–EtOAc 5:1), yields of 0.59 g (24%) for **5b** and 0.73 g (30%) for **5a** were obtained.

*10-Oxo-5*r*,6,7,8*t*,9*c*,10-hexahydro-5,9-methanobenzocyclooctene-8-carboxylic acid* (**4b**). **5b** (2.44 g, 0.01 mol) in NaOH solution (10%, 20 ml) was stirred for 3 h at 50 °C. After being cooled, the solution was acidified with concentrated HCl to pH 3, then extracted with $CHCl_3$ (3 × 30 ml); the extract was washed with water (2 × 50 ml) and dried (Na_2SO_4). On evaporation, the residue was crystallized from Et_2O–*n*-hexane, m.p. 135–137 °C, yield 2.02 g (88%). Analytical data: found C 72.9; H 5.9. Calc. for $C_{14}H_{14}O_3$: C 73.0; H 6.1%.

*5*r*,6,7,8*c*,9*c*,10-* (**6a**) *and 5*r*,6,7,8*t*,9*c*,10-hexahydro-5,9-methanobenzocyclooctene-8*t*-carboxylic acid* (**6b**). The oxo acid **4a** (2.30 g, 0.01 mol) and hydrazine hydrate (98%, 1.53 g, 0.03 mol) were added to a solution of KOH (1.68 g, 0.03 mol) in diethylene glycol (15 ml) at such a rate as to keep the temperature below 100 °C. The mixture was then heated for 1 h at 110 °C. The temperature was then raised slowly to 200 °C and maintained there for 4 h, during which time some hydrazine–water mixture distilled off. After being cooled, the mixture was added to water and the pH was adjusted to 2. Following extraction with $CHCl_3$ (3 × 50 ml), the extract was washed with water (2 × 50 ml) and dried (Na_2SO_4), and the $CHCl_3$ was evaporated off. Crystallization from *n*-hexane yielded a mixture of isomers **6a** and **6b** (1:2). Separation of a 60 mg sample by HPLC and crystallization from CH_2Cl_2–*n*-hexane, yielded **6a**: m.p. 110–112 °C, yield 34 mg (56%) and, from *n*-hexane **6b**: m.p. 145–148 °C, yield 20 mg (33%). Analytical data: found C 77.6; H 7.4 (**6a**) and C 77.6; H 7.4 (**6b**). Calc. for $C_{14}H_{16}O_2$: C 77.75; H 7.5%.

*5*r*,6,7,7a*c*,10a,10b*c* - Hexahydro - 5,10b - methanobenzocyclooct[9,8-cd]pyridazin-8-one* (**7**). A mixture of **4a** (0.46 g, 2 mmol) and hydrazine hydrate (98%, 0.1 g, 2 mmol) in EtOH (20 ml) was refluxed for 2 h and then evaporated. The residue was dissolved in 1,2-dichlorobenzene (10 ml) and refluxed for an additional 2 h. The crystals that separated out on cooling were filtered off by suction and recrystallized from EtOH, m.p. 238–239 °C, yield 0.29 g (65%). Analytical data: found C 74.15; H 6.15; N 12.95. Calc. for $C_{14}H_{14}N_2O$: C 74.3; H 6.2; N 13.2%.

Acknowledgements. The authors are indebted to Mrs. E. Csiszár-Makra and Mr. A. Fürjes for skilled technical assistance. Grants: OTKA 2693 and ETT T-121.

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Received April 7, 1997.