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SYNTHESIS OF OPTICALLY ACTIVE 10,11-DIHYDRO-5H-DIBENZO[a,d]CYCLOHEPTENES

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Abstract - The dicarboxylic acid **8** was synthesized from dibenzosuberone by dehydrogenation, reduction of the keto group and dicarboxylation. After resolution with cinchonine the (-)-enantiomer served as starting material for various transformation products with trans-configuration of the substituents at the 10,11-positions. Ring closure between these two groups led to the introduction of an additional homo- or heterocyclic ring. Attempted bromination of the dimethyl ester **9** of **8** gave the lactone **49** instead, LAH reduction of which resulted in formation of the corresponding ether bridge. Of both bridged compounds several derivatives have been prepared by modification of the substituent at C(11). Furthermore the products of nitration of the 5-keto derivatives **31** and **36** are described as well as some thio analogues and products containing one additional heteroring.

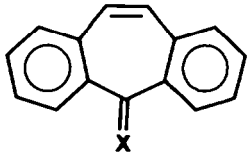
Recently we have described the chiroptical properties of several 1,2-diphenyl ethanes[1-3] and diaryl methanes[4] in which the phenyl groups can rotate. In order to fix these we have now prepared a series of optically active 10,11-dihydro-5H-dibenzo[a,d]cycloheptenes, which can serve as model compounds for both types of mentioned compounds. Their absolute configurations were determined by applying circular dichroism to ketone **25** and by X-ray diffraction of the amide **58**. In this paper we present the synthesis of these substances, their chiroptical properties will be published separately.

Commercial dibenzosuberone was radically monobrominated[5] and dehydrobrominated with triethylamine to yield ketone **1**.[5] Reduction with lithiumalanate/$AlCl_3$ led quantitatively to the known[6] olefin **2**; its 5-dideutero analogue was obtained by replacing $LiAlH_4$ by $LiAlD_4$. Following the procedure[7,8] for the dicarboxylation of phenanthrene via its 9,10-dianion the olefin **2** was treated with Na in dimethoxyethane and then with CO_2. The resulting mixture of acids was methylated and then separated by chromatography. Besides the wanted trans-diester **9**, which was formed in 31% yield, traces of the cis-diester **3** (1%) and the monoester **4** (2%) could also be isolated. Most interesting is, however, the formation of **5** in 22% yield. In order to find out whether **5** is produced by an inter- or intramolecular path the 5,5-dideutero analogue of **2** was subjected to the same reaction conditions and yielded a 3:1-mixture of **6** and **7**; the appearance of a trideutero derivative excludes at least that only intramolecular rearrangements take place. Most probably

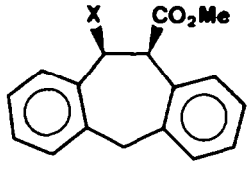
* Dedicated to Hans Wynberg on the occasion of his 65th birthday.

the rearrangement proceeds within a solvent cage on the surface of the metal.

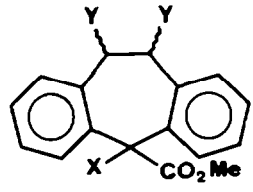
From larger batches **9** can simply be obtained in pure form and in 30% yield (calculated on basis of **2**) by crystallization from ether. It was saponified to acid **8** which could be resolved with cinchonine. From the cinchonine salt levorotatory **8** was obtained, whose enantiomeric purity was at least 98% as determined from the ^{1}H-NMR-spectrum of the monomenthylmonomethylester **11** of **8**. Partially resolved **8** obtained from the mother liquors was racemized by transformation into the dimethylester **9** and treatment of this with sodium methanolate. The free acid does not racemize even on boiling in 30% aqueous KOH. Attempts to obtain optically active material by (partial) saponification of **3** or **9** with pig liver esterase were unsuccessful.



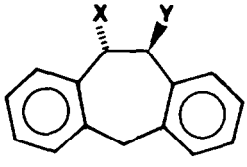
1: X = O
2: X = H_2

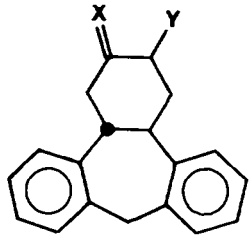


3: X = CO_2Me
4: X = H

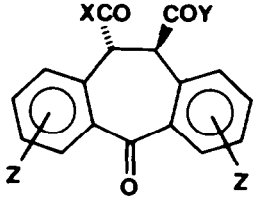


5: X = Y = H
6: X = D, Y = H
7: X = Y = D



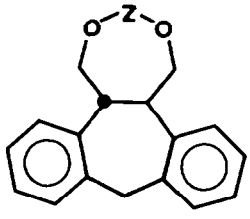


25: X = O, Y = OH
26: X = H_2, Y = H

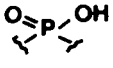


	X	Y
8:	CO_2H	CO_2H
9:	CO_2Me	CO_2Me
10:	CO_2H	CO_2Me
11:	CO_2Me	CO_2M^*
12:	CO_2H	CH_2OMe
13:	CO_2Me	CH_2OMe
14:	CO_2H	Me
15:	CO_2Me	Me
16:	CH_2OH	CH_2OH
17:	CH_2OH	CH_2OMe
18:	CH_2OMe	CH_2OMe
19:	CH_2OAc	CH_2OAc
20:	CH_2CO_2H	CH_2CO_2H
21:	CH_2CO_2Me	CH_2CO_2Me
22:	CH_2CN	CH_2CN
23:	Me	CH_2OH
24:	Me	Me

M*: Residue of (-)-menthol



27: Z 

28: Z 

29: Z 

	X	Y	Z
30:	OH	OMe	H
31:	OMe	OMe	H
32:	OMe	NHR*	H
33:	OMe	OMe	1,6-$(NO_2)_2$
34:	OMe	OMe	1,7-$(NO_2)_2$
35:	OMe	OMe	3,7-$(NO_2)_2$

R*: Residue of (R)-phenylethyl amine

10,11-Disubstituted Derivatives.

Several 10,11-disubstituted dihydrodibenzocycloheptenes were prepared from the diol **16**, which in turn was obtained from the diester **9** by reduction with excess lithium alanate in 95% yield. If only the equivalent amount of $LiAlH_4$ is used a great deal of optically inactive material resulted which is probably a hemiacetal with 10,11-cis-configuration. Methylation of **16** with dimethyl sulfate under phase-transfer catalysis led to the monoether **17** or to the dimethylether **18**, depending on the amount of reagent.

Acetylation of **16** gave the diacetate **19**, complete tosylation a ditosylate, which was reacted further without special purification. Its reduction with lithium alanate gave in 52% yield the wanted hydrocarbon **24**, accompanied by 5% of the alcohol **23** and a greater amount of diol **16**. In better yield **23** can be obtained by $LiAlH_4$-reduction of the monotosylate of **16**; appreciable amounts of the diol **16** are produced also in this reaction. Replacement of the tosyloxy groups by CN gave in 63% yield the dinitrile **22**. The corresponding dicarboxylic acid **20** was obtained by acidic saponification and was further characterized by its dimethyl ester **21**.

Jones oxidation of the monoether **17** gave the acid **12** in 46% yield, which was methylated with diazomethane to its ester **13**. In similar manner the alcohol **23** was transferred into the acid **14** (68% yield) and its methyl ester **15**.

In order to rigidify the system a few ring-closed derivatives of such disubstituted dibenzocycloheptenes were synthesized. The alicyclic compound **25** could be prepared by acyloin condensation of the diester **21** in 40 to 55% yield when xylene was used as the solvent; in toluene only 25% could be obtained.[9] The intermediate enediol disilylether was not isolated but hydrolysed directly to the acyloin **25**. Reduction of the hydroxy group with Zn in acid[10] and subsequent removal of the carbonyl group by the Huang Minlon modification of the Wolff-Kishner reduction gave then in 50% overall yield the hydrocarbon **26**.

The heterocyclic derivatives **27** to **29** were synthesized from the diol **16** by conventional methods. $SOCl_2$ in methylene chloride and triethylamine as catalyst gave in 94% yield the cyclic sulfite **27**, analogous reaction with $POCl_3$ and further hydrolysis of the acid chloride yielded the cyclic acidic phosphate **28**. The cyclic acetonide **29** was prepared by transacetalation with 2,2-dimethoxypropane and toluenesulfonic acid as catalyst in 86% yield. All these optically active compounds have been fully characterized by their spectral data.

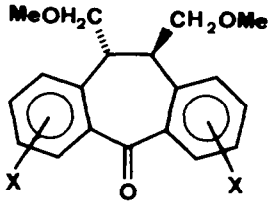
5-Keto Derivatives and their Reaction products.

The direct oxidation of **9** to its 5-keto derivative with SeO_2 in acetic anhydride[11] proceeded only with poor yield and was much better achieved via the lactone **49** (described below) by Jones oxidation. Reaction with CH_2N_2 gave the corresponding dimethyl ester **31**. The amide **32** was obtained from **30** and (+)-phenylethylamine with dicyclohexyl carbodiimide with the intention to determine its absolute configuration by X-ray diffraction.

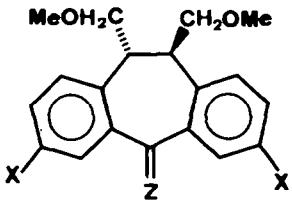
31 was treated with 95% HNO_3 without any solvent[12] in order to obtain products substituted in the aromatic ring(s). Indeed, three nitro-compounds (**33** - **35**) could be isolated, they were, however, optically inactive. Obviously under the strongly acidic conditions protonation of the CO_2Me and/or keto group takes place with simultaneous removal of the protons at 10/11-positions which leads to racemization. The positions of the NO_2-groups follow from the patterns of the signals of aromatic protons in the ^1H-NMR-spectra.

In order to avoid deprotonation in the C_2-bridge a similar nitration was successfully tried on the ketone **36** which could be obtained in excellent yield from the diether **18** by oxidation with $KMnO_4$ in heterogeneous phase.[13] The main product of the nitration[12] was the symmetrical dinitro-compound **38** (42%), accompa-

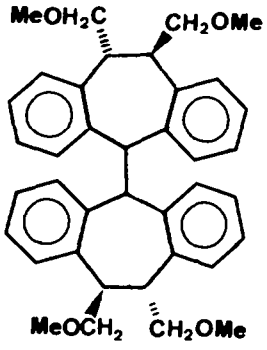
nied by **37** (22%) and the 3,6-isomer **39** (11%). A nitration in o-position to the usually m-directing carbonyl group is not without precedent.[14] The positions of the NO_2-groups were again determined from the ^{1}H-NMR-spectra.



	X
36:	H
37:	1,7-$(NO_2)_2$
38:	3,7-$(NO_2)_2$
39:	3,6-$(NO_2)_2$



	X	Z
40:	H	H,OH
41:	H	Me,OH
42:	H	H_2C
43:	NH_2	O
44:	NHAc	O
45:	NH_2	H_2
46:	NHAc	H_2
47:	OAc	H_2



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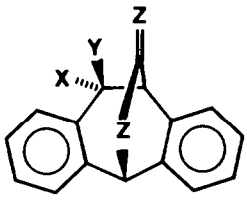
Reduction of the NO_2-groups of **38** had to be done under conditions which avoid possible racemization and simultaneous reduction of the keto group. It was achieved by reaction with $SnCl_2$ in acetic acid containing conc. HCl.[15] The resulting diamine **43** was transformed into the diacetate **44** under standard conditions, and into the deoxo derivative **45** by reduction with $LiAlH_4/AlCl_3$. It is remarkable that **45** is also obtained with Zn in acetic acid/HCl mixture, but with partial racemization. The N,N-diacetate **46** was prepared, again under the usual conditions, and the transformation of the amino groups into OH was done by diazotisation and boiling of the diazonium salt in 50% sulfuric acid containing sodium sulfate. Since the diphenol is very unstable it was not isolated in pure form but acetylated immediately to **47**. If the diazotisation is carried out in absence of urea appreciable amounts of nitrosophenols are formed as byproducts. Analogous reductions of the nitrocompounds **37** and **39** have not yet been tried.

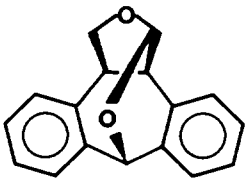
Since the keto-function is the only reactive group in **36** it could be transformed into a few others without difficulty. Reduction with $LiAlH_4$ led to the alcohol **40**. All attempts to replace its hydroxyl by chlorine or fluorine gave only the cyclic ether **61**, which is described later. The 5-methyl homologue **41** of **40** was obtained from **36** with Grignard reagent. With thionyl chloride in pyridine **41** was smoothly dehydrated to the methylene ketone **42**. Under conditions of the McMurry reaction[16] a dimer was obtained, it was, however, not the expected olefin but the corresponding dihydro derivative **48**. Only a single stereoisomer can exist with this structure since no new elements of chirality are generated by the coupling reaction.

Lactones Derived from 5-Hydroxy compounds.

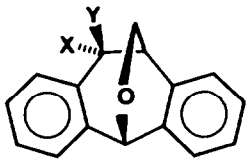
Radical bromination of the diester **9** did not give any bromo-compound but the lactone **49** instead. Initial radical formation proceeds in 5-position since this is benzylic with respect to both aromatic rings, and whatever is the intermediate conformation, one of the two methoxycarbonyl groups is always in close distance for ring closure. Saponification of **49** gave the monoacid **50**, with P_4S_{10} in xylene



	X	Y	Z
49:	CO_2Me	H	O
50:	CO_2H	H	O
51:	H	CH_2OH	O
52:	CO_2Me	H	S



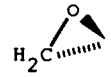
53



	X	Y
54:	CO_2H	H
55:	CO_2Me	H
56:	$CONH_2$	H
57:	CONHR*	H
58:	CONMeR**	H
59:	CH_2OH	H
60:	CH_2OAc	H
61:	CH_2OMe	H
62:	CH_2F	H
63:	CN	H
64:	Me	H
65:	OH	H
66:	OPhth	H
67:	H	OH
68:	H	OPhth
69:	H	H
70:	=O	
71:	$=CH_2$	

72:

73:



R**: Residue of (-)-ephedrine
Phth: hemiphthalate

the dithiolactone **52** can be obtained. Reaction of the lactone **49** with $NaBH_4$ in methanol[17] resulted in the partial reduction of the methoxycarbonyl group under epimerization leading to **51**. The configuration at the C_2-bridge of **51** was proved by chemical correlation with the cis-anhydride **80** (cf. Experimental Part). We assume that this epimerization takes place at the intermediary aldehyde stage. The acetal **53**, isolated as a byproduct, is formed nearly exclusively when lithium-borohydride in THF is used as the reagent. The structure of **53** follows from its spectra and especially from a DEPT-experiment showing a ^{13}C-chemical shift of 101 ppm, typical for an acetal-C.

5,10-Oxaethano-bridged Systems.

Reduction of the ester-lactone **49** with $LiAlH_4$ in THF/ether mixture did not give the expected triol but the cyclic ether **59** although no Lewis acid had been added. The same product is also accessible by NBS-oxidation of the diol **16** in CCl_4, but in lower yield. Acetylation of **59** with acetic anhydride led to the acetate **60**, methylation under phase - transfer conditions to the diether **61**. Oxidation with Jones reagent gave, besides the acid **54** (57%), also the nor-ketone **70** (39%). The acid chloride of **54**, prepared with oxalyl chloride, was used to synthesize the amide **56** as well as the chirally substituted amides **57** and **58**, whereas the methyl ester **55** was obtained from the acid with diazomethane. Dehydration of the amide **56** yielded 58% of the nitrile **63**. For the preparation of the methyl derivative **64** the tosylate of **59** was reduced with lithium alanate without purification of that intermediate. Replacement of OH for F did not proceed with NaF via the tosylate, nor directly by Olah's reagent. It could, however, be achieved with SF_4 in benzene at 60°C (**62**).

From the norketone **70** the deoxygenated compound **69** was obtained by Wolff-Kishner reduction, and a mixture of the two alcohols **65** and **67** by alanate reduction. Their stereochemistry was determined from NOE-difference spectra (observation of the signal of one H of the oxaethano-methylene group when irradiating the H geminal to OH), and they could be separated completely by silicagel chromatography (48% **65**, 45% **67**). The corresponding hemiphthalates were obtained by treatment with phthalic anhydride.

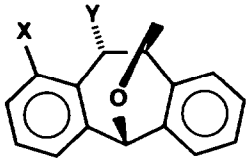
The styrene **71** was prepared by elimination of toluenesulfonic acid from the tosylate of **59** by heating with KOH to 200°C in 84% yield. Epoxidation led to a mixture of the two oxido derivatives **72** and **73** together with some ketone **70**. **72** could be isolated in pure form by silicagel chromatography (36%), its diastereomer **73** was obtained purely by crystallization from ether. Its yield (35%) was determined by integration of the signal of the proton at C(5) in the mixture with **70** (12%). The stereochemistry of the oxido compounds was again determined from NOE-difference measurements between the nearer protons of each methylene group next to the ether oxygens.

Some Further Derivatives.

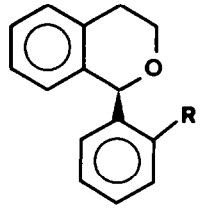
Monosubstitution at C(1) was achieved via isochromane formation with chloromethyl methyl ether and $ZnCl_2$ from **59**, leading to **75** in 95% yield. Oxidation of the latter with Jones reagent to **76** proceeded much better than with CrO_3 in DMF. P_4S_{10} transformed **76** into the dithiolactone **77** (61%), alanate reduction gave the diol **74** (92%). An attempted reduction of its benzylic OH by $LiAlH_4/AlCl_3$ led to quantitative recovery of the isochromane **75**.

The cleavage product **78** was prepared with the intention to determine the absolute configuration via the CD of an isochromane by reaction of **70** with potassium tert.-butylate in DMSO.[18] No product of the splitting of the bond between the carbonyl and the benzene ring could be observed. Reduction to the benzylic alcohol **79** with alanate proceeded smoothly and in good yield (94%).

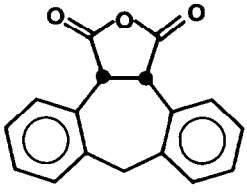
Attempts to prepare the trans-anhydride from the dicarboxylic acid **8** under various conditions gave solely the cis-product **80**, with epimerization. The cis-dimethylester **3** and the corresponding monoester react with NBS in a similar manner as their trans-analogues to form the lactone **81** in good yield.



	X	Y
74:	HOH_2C	CH_2OH
75:	$-CH_2-O-CH_2-$	
76:	$-C(=O)-O-CH_2-$	
77:	$-C(=S)-S-CH_2-$	



78: R = CO_2H
79: R = CH_2OH



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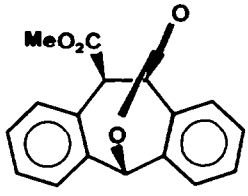

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EXPERIMENTAL

General

The melting points were determined with a heating microscope (Fa. Reichert) and are not corrected. Optical rotations were measured with a Perkin-Elmer 141 in cells of 10 cm lengths; concentrations are given in mg/ml. The NMR-spectra were recorded with a WP 80 or an AM 400 (Fa. Bruker). The chemical shifts are given in ppm and refer to the δ-scale. The signal multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. IR-spectra were measured with a Perkin-Elmer 257 in chloroform solution or in KBr-pills, wave-numbers are cited only for characteristic functional groups. A MAT CH-5 (Fa. Varian) was used for recording the mass-spectra (70 eV). The UV-spectra were taken with a Cary 17 (Fa. Varian) in cells of 0.01 - 2 cm lengths.

General work-up: the organic phase was washed neutral with aqueous HCl or H_2SO_4 and/or saturated aqueous $NaHCO_3$ and water, dried over $MgSO_4$ and brought to dryness in vacuo. Usually the resulting residue was then chromatographed on silicagel (particle size 0.05 - 0.1 mm).

Abbreviations: DCC = dicyclohexylcarbodiimide, DMAP = dimethylaminopyridine, DMSO = dimethyl sulfoxide, PE = petrol ether (60-70°C), THF = tetrahydrofuran. **DBCH** = 10,11-dihydro-5H-dibenzo [a,d]cycloheptene.

Dibenzo[a,d]cyclohepten-5-one (**1**).

1 was prepared according to the procedure of Cope and Fenton.[5] M.p. 87 - 88°C. ^{1}H-NMR (80 MHz, $CDCl_3$): 6.9 (s, 2H, -CH=CH-), 7.3 - 7.6 (m, 6H, arom. H), 8.0 - 8.3 (m, 2H, arom H). IR ($CHCl_3$): 3000, 1640 (CO), 1590 cm^{-1}. MS: m/z (%) = 206 (73, M^+), 178 (100, $(M - CO)^+$).

Dibenzo a,d cycloheptene (**2**).

To a suspension of 40 g (1.026 mol) $LiAlH_4$ in 500 ml ether a solution of 137 g (1.026 mol) $AlCl_3$ in 700 ml ether was added dropwise. After 10 minutes 191 g (0.918 mol) **1** (dissolved in 1 l THF) were added and the mixture was refluxed for 2 h. After cooling to 0°C 1.3 l water were added. The precipitate was dissolved in aqueous 10% H_2SO_4. General work-up gave 177 g of **2** (quantitative yield), m.p. 129°C (lit.[6]: 131°C). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.65 (s, 2H, $-CH_2-$), 6.8 (s, 2H, -CH=CH-), 7.0 - 7.2 (m, 8H, arom. H). IR (in $CHCl_3$): 3020, 2980 cm^{-1}. MS: m/z (%) = 192 (100, M^+), 191 (90, $(M - H)^+$), 165 (12, diphenylmethane cation).

Carboxylation of alkene **2** to **3**, **4**, **5**, and **9**.

A solution of 6.703 g **2** (0.035 mol) in 100 ml dry dimethoxyethane was cooled to 0°C and dry nitrogen was passed to remove air. Thin strips of 6 g freshly cut sodium (oxide free) were added. After a few minutes a dark brown mossy precipitate was formed on the metal surface. The pale brown solution was then stirred for 3 h at 0°C, becoming rapidly dark brown. Afterwards a stream of dry carbon dioxide was passed over the surface of the reaction mixture for 15 min., leading to decolouration. The solution was then decanted, and the rest of the sodium pieces was washed with some ml THF. The mixture was evaporated in vacuo and the residue was dissolved in 150 ml 1 N NaOH. After washing 3 times with 80 ml ether the aqueous phase was acidified with 10% HCl, followed by extraction with ether (80 ml, 3 times). The organic phase was dried over $MgSO_4$, the filtrate was cooled to 0°C and ethereal diazomethane (excess) was added. The usual work-up gave a mixture of four methyl esters, which were separated by chromatography (PE/ethyl acetate 10:1): **3** (130 mg, 1%), **4** (170 mg, 2%), **5** (1.93 g, 22%), **9** (3.36 g, 31%).

Dimethyl cis-DBCH-10,11-dicarboxylate (**3**): Oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.8 (s, 6H, two $-OCH_3$), 4.1 (AB system, 2H, $-CH_2-$), 4.7 (s, 2H, two arCH-COO), 7.0 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 1730 (ester), 1480, 1430 cm^{-1}. MS: m/z (%) = 310 (13, M^+), 250 (45), 191 (100).

Methyl DBCH-10-carboxylate (**4**): Oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.3 - 3.8 (AB part of an ABX system, 2H, CH_2 (11)), 3.6 (s, 3H, $-OCH_3$), 4.1 (AB system, 2H, ar-CH_2-ar), 4.2 (X part of an ABX system, 1H, H(10)), 7.0 - 7.3 (m, 8 H, arom. H). IR ($CHCl_3$): 1720 (ester), 1480, 1150 cm^{-1}. MS: m/z (%) = 252 (11, M^+), 220 (3, $(M-CH_3OH)^+$), 191 (100), 178 (21).

Methyl DBCH-5-carboxylate (**5**): m.p. 91 - 92°C. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.65 - 3.5 (AA'BB' system, 4H, $-CH_2-CH_2-$), 3.65 (s, 3H, $-OCH_3$), 4.75 (s, 1H, ar_2-CH-COO), 7.1 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 1740 (ester), 1490 cm^{-1}. MS: m/z (%) = 252 (13, M^+), 193 (100, $(M-CO_2CH_3)^+$), 178 (21), 115 (23).

Dimethyl trans-DBCH-dicarboxylate (**9**): m.p. 128 - 129 °C (PE/ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.75 (s, 6H, two $-OCH_3$), 4.1 (s, 2H, $-CH_2-$), 4.8 (s, 2H, two arCH-COO), 7.2 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2990, 1740 (CO) ,1480, 1430 cm^{-1}. MS: m/z (%) = 310 (8, M^+) 278 (10, $(M -CH_3OH)^+$), 250 (43, $(M -HCO_2 CH_3)^+$), 218 (5), 191 (100, dibenzotropylium cation).

Carboxylation of the 5,5-dideutero analogue of **2** to **6** and **7**.

The 5,5-dideutero analogue of **2** was prepared from **1** with $LiAlD_4$ as described for **2**. Its carboxylation was performed as above; work-up gave a mixture of **6** and **7**. Their ratio was determined from the intensity ratio of the parent peaks in the mass-spectrum: 14 % m/z = 253 (**6**), 5 % m/z = 255 (**7**).

Preparation of **9** in larger scale.

THF can be used as a cosolvent without effecting the yield of **9**: 22 g (114.6 mmol) **2** in a mixture of 180 ml dimethoxyethane and 140 ml THF were treated with 16 g sodium (687 mmol) and carbon dioxide as described above. The combined mixture of acids prepared from 176 g of **2** (8 experiments with 22 g of **2** each) was esterified with diazomethane in ether and the solution concentrated in vacuo. The dimethyl ester could be obtained by crystallization (cooling overnight to -20°C), yielding 86 g (30 %) of **9**.

DBCH-10,11-dicarboxylic acid (8).

To a boiling solution of 86 g (0.277 mol) **9** in 400 ml methanol were added dropwise 400 ml 20 % aqueous KOH and simultaneously methanol/water was distilled off. After 400 ml solvent had been removed the reaction mixture was cooled to room temperature and diluted with 400 ml water. After washing two times with 100 ml ether the aqueous phase was acidified with conc. HCl and worked up: 78.2 g of **8** (quantitative yield), m.p. 213 - 214°C (ether). ^{1}H-NMR (80 MHz, acetone-d6): 3.45 (s, 2H, -CH_2-), 4.1 (s, 2H, two ar$\underline{CH}$-COO), 6.3 - 6.7 (m, 8H, arom. H), 8.3 - 8.9 (broadened s, 2H, two COOH). IR (KBr): 3640 - 2200 (OH), 1690 (CO), 1490, 1410 cm^{-1}. MS: m/z (%) = 282 (13, M^+), 264 (20, $(M-CO)^+$), 236 (44), 191 (100, dibenzotropylium cation).

Resolution of **8**.

To a hot solution of 78.2 g (0.277 mol) **8** in 780 ml 80% aqueous acetone were added 82 g (0.277 mol) cinchonine and the mixture was refluxed for 1 h. After addition of 200 ml water refluxing continued for 3 h. Slow cooling over night gave 61.2 g salt, which after one further crystallization from 1.1 l ethanol yielded 48.5 g salt of m.p. 198°C. This was suspended in 300 ml cold (0°C) water, then 300 ml ether were added and 10% aqueous HCl until the solution became clear. Separation of the organic phase and general work-up gave 23.7 g of (-)-**8** (60%), m.p. 258°C (ether). $[\alpha]_D^{23}$ = -116 (c = 2, dioxane).

Racemization of combined mother liquors of **8**: The combined mother liquors were evaporated in vacuo and the residue was acidified with HCl. Extraction with ether and evaporation of the dried ether phase yielded 53 g of acid **8**, which was esterified by refluxing in 400 ml methanol containing 8 ml conc. H_2SO_4 for 10 h. An excess of sodium methanolate was added and reflux was continued for 2 h. Saponification as described above yielded 52 g of racemic **8**.

Dimethyl (10R,11R)-DBCH-10,11-dicarboxylate ((-)-**9**).

A solution of 23.7 g (84 mmol) (-)-**8** in 300 ml ether was cooled to 0°C and stirred for 1 h after addition of an excess of etherial diazomethane. Work-up gave (-)-**9** in quantitive yield, m.p. 82°C (ether). $[\alpha]_D^{25}$ = -100 (c = 2, dioxane).

Methyl (10R,11R)-10-carboxy-DBCH-11-carboxylate (**10**).

To a cooled solution of 282 mg (1 mmol) (-)-**8** in 30 ml ether was added dropwise etherial diazomethane under thin layer chromatographic control (until formation of **9**). Work-up and chromatography (PE/acetone 4:1, 1% acetic acid) yielded 214 mg of **10** (72%), m.p. 159 - 160°C (racemate; ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.7 (s, 3H, -OCH_3), 4.0 - 4.1 (AB-system, 2H, ar-$\underline{CH}_2$-ar), 4.7 (s, 2H, two ar$\underline{CH}$-COO), 7.0 - 7.3 (m, 8H, arom. H), 10.5 (s, 1H, COOH). IR ($CHCl_3$): 3500 - 2500, 1725, 1490, 1430, 1280 cm^{-1}. MS: m/z (%) = 296 (8, M^+), 264 (10), 236 (34), 191 (100), 165 (11).

(ℓ)-Menthyl methyl (10R,11R)-DBCH-10,11-dicarboxylate (**11**).

A solution of 150 mg (0.51 mmol) monomethyl ester (-)-**10** and 10 mg DMAP in 1 ml CH_2Cl_2 was cooled to 0°C and 5 min. stirred at that temperature after addition of 125 mg (0.61 mmol) DCC. After further stirring for 4 h at room temperature 20 ml CH_2Cl_2 were added, the organic phase was washed with 10 ml of 5% aqueous HCl and worked up. After chromatography with PE/ethyl acetate (10:1) 206 mg (94%) of **11** were obtained as colourless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.70 and 0.80 (d/d, 6H, CH($\underline{CH}_3$)$_2$), 0.90 (d, 3H, CH_3), 0.80 - 1.10 (m, 4H), 1.20 - 1.50 (m, 2H), 1.60 - 1.80 (m, 1H) 2.00 (m, 1H), all from menthyl, 3.75 (s, 3H, OCH_3), 4.10 (s, 2H, ar-$\underline{CH}_2$-ar), 4.70 - 4.85 (m, 3H, H(10), H(11) and -$CO_2\underline{CH}$-), 7.05 - 7.20 (m, 8H, 8 arom. H). IR ($CHCl_3$): 1735 cm^{-1} (ester). MS: m/z (%) = 434 (3, M^+), 296 (64, (M - menthyl)$^+$), 250 (51), 236 (92), 191 (90), 83 (100).

Determination of enantiomeric purity of **11**.

The menthyl methyl ester **11** was used for the determination of the enantiomeric purity of (-)-**8** by integration of the carbomethoxy signal in the 400 MHz ^{1}H - spectrum. The spectrum of the mixture of diastereomeric esters prepared from racemic **8** showed a separation for the -$COOCH_3$ signals of 9 Hz (integration ratio 1:1). If **11** was prepared from (-)-**8** a ratio of 99:1 was obtained for the integration of the carbomethoxy signals (e.e. > 98%).

(10R,11R)-10-Methoxymethyl-DBCH-11-carboxylic acid (**12**).

To 240 mg (0.94 mmol) **17** in 15 ml acetone were added 3 ml Jones reagent (8N). After stirring 1 h at room temperature 2 ml ethanol were added. The solution was concentrated in vacuo and the re-

sidue suspended in 50 ml water. After extraction with ether (30 ml, 3 times) and general work-up, chromatography (PE/ethyl acetate 6:1, 1% acetic acid) yielded 121 mg of **12** (46%) as glassy material. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.3 (s, 3H, $-OCH_3$), 3.1 - 3.9 (m, 3H, ar$\underline{CH}$-$\underline{CH_2}$), 3.95 - 4.2 (m, 1H, ar$\underline{CH}$-COO), 4.2 - 4.4 (m, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.4 (m, 8H, arom. H), 9.1 (broad s, 1H, COOH). IR (KBr): 3500 - 2400 (OH), 1705 (CO), 1490, 1115 cm^{-1}. MS: m/z (%) = 282 (8, M^+), 250 (86, $(M-MeOH)^+$), 205 (97), 191 (100), 178 (60), 45 (93, $CH_3-O\underline{CH_2}^+$).

Methyl (10R,11R)-10-methoxymethyl-DBCH-11-carboxylate (**13**).

78 mg **12** were esterified with etherial diazomethane in the usual way. Chromatography (PE/ethyl acetate 10:1) yielded 78 mg of **13** (96%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.3 (s, 3H, $-OCH_3$), 3.85 (s, 3H, $-COOCH_3$), 3.1 - 3.9 (m, 3H, ar$\underline{CH}$-$\underline{CH_2}$-), 3.95 - 4.2 (m, 1H, ar$\underline{CH}$-COO), 4.2 - 4.4 (AB-system, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.4 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2940 - 2840, 1735 (CO), 1500, 1440, 1210, 1120 cm^{-1}. MS: m/z (%) = 296 (3, M^+), 264 (49, $(M-MeOH)^+$), 232 (25), 205 (78), 191 (100).

(10R,11R)-10-Methyl-DBCH-11-carboxylic acid (**14**).

To a solution of 208 mg (0.87 mmol) **23** in 15 ml acetone were added dropwise 5 ml Jones reagent (8N). After stirring 1 h at room temperature ethanol was added and the solvent evaporated in vacuo. The residue was suspended in 40 ml water and extracted with ether (20 ml, 3 times). Work-up and chromatography (PE/acetone 8:1, 1 % acetic acid) gave 150 mg of **14** (68%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.4 (d, 3H, $-CH_3$), 3.7 - 3.85 (m, 1H, ar$\underline{CH}$-), 3.8 - 4.05 (AB-system, 2H, ar-$\underline{CH_2}$-ar), 4.5 (m, 1H, ar$\underline{CH}$-COO), 7.0 - 7.3 (m, 8H, arom. H), 10.9 (broad s, 1H, COOH). IR ($CHCl_3$): 3550 - 2500 (OH), 1700 (CO), 1480 cm^{-1}. MS: m/z (%) = 252 (40, M^+), 206 (100), 191 (89), 178 (69), 165 (24).

Methyl (10R,11R)-10-methyl-DBCH-11-carboxylate (**15**).

103 mg (0.39 mmol) **14** were esterified with etherial diazomethane in the usual way. Work-up yielded 108 mg of **15** (quantitative) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.4 (d, 3H, $-CH_3$), 3.75 - 3.85 (m, 1H, ar$\underline{CH}$-), 3.8 - 4.05 (AB-system, 2H, ar-$\underline{CH_2}$-ar), 3.85 (s, 3H, $COCH_3$), 4.5 (m, 1H, ar$\underline{CH}$-COO), 7.05 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3060 - 2940, 1725 (ester), 1480, 1450, 1310 cm^{-1}. MS: m/z (%) = 266 (1.5, M^+), 206 (13, $M-HCO_2CH_3)^+$), 191 (11), 178 (6), 117 (100).

(10R,11R)-10,11-Bishydroxymethyl-DBCH ((+)-**16**).

To a suspension of 7.75 g (198.7 mmol) $LiAlH_4$ in 100 ml ether a solution of 20.03 g (64.6 mmol) **9** in 200 ml THF was added dropwise and refluxed for 2 h. After cooling to 0°C 200 ml water were added and the solution was acidified with 10% aqueous H_2SO_4. General work-up and crystallization from ether yielded 15.59 g of **16** (95%). M.p. 149°C (ether). $[\alpha]_D^{25}$ = +42 (c = 2, dioxane). ^{1}H-NMR (80 MHz, DMSO-d6): 3.3 - 3.8 (m, 6H, two ar-$\underline{CH}$-$\underline{CH_2}$-), 4.0 (s, 2H, ar-$\underline{CH_2}$-ar), 4.7 (t, 2H, two -OH), 6.9 - 7.2 (m, 8H, arom. H). IR (KBr): 3500 - 2600 (OH), 1450, 1050, 1020 cm^{-1}. MS: m/z (%) = 236 (39, $(M-H_2O)^+$), 205 (100), 193 (56). Found: C, 80.32%; H, 7.11%. $C_{17}H_{18}O_2$ requires C, 80.28%; H, 7.13%.

If stoichiometric amounts of $LiAlH_4$ were used an optically inactive material (hemiacetal, ?) was isolated as the main product. MS: m/z (%) = 252 (M^+), positive test with dinitrophenyl hydrazine.

(10R,11R)-10-Hydroxymethyl-11-methoxymethyl-DBCH (**17**).

To a vigorously stirred mixture of 794 mg (3.13 mmol) **16** 50 mg tetra-n-butylammonium bromide in 10 ml methylene chloride and 10 ml 50% aqueous NaOH were added 400 mg (3.27 mmol) dimethyl sulfate. After stirring 10 min. at room temperature 200 ml water were added, followed by extraction with methylene chloride (50 ml, 2 times). Work-up and chromatography (PE/acetone 10:1) yielded 771 mg of **17** (92 %) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.3 (broad s, 1H, -OH), 3.0 - 3.8 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 3.25 (s, 3H, $-OCH_3$), 4.05 - 4.2 (m, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3600, 3420, 2940 - 2880, 1490, 1460, 1120 cm^{-1}. MS: m/z (%) = 250 (8, $(M-H_2O)^+$), 236 (43), 218 (27), 205 (100), 191 (45), 179 (45).

(10R,11R)-10,11-Bismethoxymethyl-DBCH (**18**).

To a vigorously stirred mixture of 1.2 g (4.72 mmol) **16**, 100 mg tetra-n-butylammonium bromide, 15 ml methylene chloride, and 15 ml 50% aqueous NaOH were added 6 ml dimethyl sulfate and the emul-

sion was heated to 50°C for 5 h. Afterwards another 4 ml dimethyl sulfate were added and stirring was continued for 5 h at 50°C. Dilution with 200 ml water, extraction with methylene chloride, work-up and chromatography (PE/ethyl acetate 15:1) gave 1.264 g of **18** (95%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.1 (s, 6H, two $-OCH_3$), 3.2 - 3.7 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 4.0 (s, 2H, ar-$\underline{CH_2}$-ar), 6.8 - 7.1 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2940 - 2820, 1490, 1450, 1110 cm^{-1}. MS: m/z (%) = 250 (37, $(M-CH_3OH)^+$), 218 (25), 205 (92), 191 (39), 179 (27), 45 (100).

(10R,11R)-10,11-Bisacetoxymethyl-DBCH (19).

To a solution of 167 mg (0.66 mmol) **16**, 10 mg DMAP and 0.3 ml triethylamine in 1 ml dioxane were added 0.5 ml acetic anhydride. After stirring 30 min. at room temperature the solvent was evaporated in vacuo and the residue purified by chromatography (PE/ethyl acetate 8:1): 209 mg of **19** (94%), colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.0 (s, 6H, two $COCH_3$), 3.4 - 3.65 (m, 2H, two ar$\underline{CH}$-), 3.95 - 4.50 (m, 4H, -$\underline{CH_2}$OAc), 4.2 (s, 2H, ar-$\underline{CH_2}$-ar), 7.05 - 7.30 (m, 8H, arom. H). IR ($CHCl_3$): 3010, 2960, 1740 (CO), 1500, 1370, 1240 cm^{-1}. MS: m/z (%) = 278 (25, $(M-CH_3COOH)^+$), 218 (100), 205 (58), 191 (29).

(10R,11R)-10,11-Biscarboxymethyl-DBCH (20).

A mixture of 1.03 g (3.73 mmol) **22** in 9 ml conc. H_2SO_4, 9 ml water and 15 ml acetic acid was refluxed for 6 h. The reaction mixture was poured onto 200 g ice, followed by extraction with ether (60 ml, 3 times). The solvent was evaporated in vacuo and the residue dissolved in 75 ml 10% aqueous KOH. After washing with 50 ml CH_2Cl_2 (3 times) the aqueous phase was acidified with HCl and extracted with ether (50 ml, 3 times). Work-up and crystallization from PE/acetone yielded 810 mg of **20** (70%), m.p. 134°C (PE/acetone), ^{1}H-NMR (80 MHz, acetone-d6): 2.45 - 2.65 (m, 4H, two -$\underline{CH_2}$COO), 3.6 - 3.85 (m, 2H, two ar$\underline{CH}$-), 4.3 (s, 2H, ar-$\underline{CH_2}$-ar), 7.1 - 7.35 (m, 8H, arom. H). IR (KBr): 3600 - 2400 (OH), 1700 (CO), 1490, 1410, 1260. MS: m/z (%) = 310 (0.2, M^+), 292 (23, $(M-H_2O)^+$), 250 (62), 191 (100).

(10R,11R)-DBCH-10,11-bisacetic acid dimethyl ester (21).

810 mg **20** were esterified with etherial diazomethane as usual. Work-up and chromatography (PE/ethyl acetate 10:1) yielded 841 mg of **21** (quantitative) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.4 - 2.6 (m, 4H, two -$\underline{CH_2}$-COO), 3.5 (s, 6H, two $-OCH_3$), 3.5 - 3.9 (m, 2H, two ar$\underline{CH}$-), 4.3 (s, 2H, ar-$\underline{CH_2}$-ar). IR ($CHCl_3$): 3010, 2950, 1730 (CO), 1440, 1165 cm^{-1}. MS: m/z (%) = 338 (2, M^+), 306 (35, $(M-CH_3OH)^+$), 264 (72), 205 (42), 191 (100), 178 (18).

(10R,11R)-10,11-Biscyanomethyl-DBCH (22).

From 2.495 g (9.82 mmol) **16** and 4.13 g (21.6 mmol) p-toluenesulfonyl chloride was prepared the ditosylate (95%, cf. **34**). The crude ditosylate was dissolved in 10 ml dimethyl sulfoxide and added dropwise to a hot (95°C) suspension of 1.43 g (27.8 mmol) NaCN (dry) in 18 ml DMSO. The mixture was stirred 1 h at 95°C, cooled to room temperature and poured into 500 ml 3% aqueous NaOH. After extraction with 70 ml ether (3 times) and work-up the product was purified by chromatography (PE/ethyl acetate 7:1): 1.62 g of **22** (63%), m.p. 163°C (PE/ethyl acetate). ^{1}H-NMR (80 MHz, $CDCl_3$): 2.4 - 2.7 (m, 4H, two -$\underline{CH_2}$-CN), 3.5 - 3.8 (m, 2H, two ar$\underline{CH}$-), 4.25 (s, 2H, ar-$\underline{CH_2}$-ar), 7.1 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3010, 2250 (CN), 1500, 1440, 1240 cm^{-1}. MS: m/z (%) = 272 (14, M^+), 231 (4, $(M-CH_3CN)^+$), 205 (4), 191 (100), 178 (5).

(10R,11R)-10-Hydroxymethyl-11-methyl-DBCH (23).

To a cooled (0°C) solution of 756 mg (2.98 mmol) **16** in 10 ml pyridine were added 570 mg (2.98 mmol) p-toluenesulfonyl chloride. After stirring 3 h at room temperature the reaction mixture was poured onto ice followed by acidification (HCl) and extraction with CH_2Cl_2 (60 ml, 2 times). The organic phase was washed twice with 5% aqueous HCl and water, dried over $MgSO_4$ and evaporated in vacuo. The residue was dissolved in 20 ml THF and the solution added dropwise to a suspension of 250 mg (6.4 mmol) $LiAlH_4$ in 40 ml ether. The mixture was refluxed for 1 h and worked up as usual. Chromatography (PE/ethyl acetate 6:1) yielded 205 mg of **23** (29%), m.p. 75 - 76°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.4 (d, 3H, $-CH_3$), 2.9 - 3.9 (m, 5H, two ar$\underline{CH}$- and -$\underline{CH_2}$OH), 4.1 (AB-system, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2990, 2880, 1490, 1060, 920 cm^{-1}. MS: m/z (%) = 236 (100 $(M-H_2)^+$), 205 (64), 191 (57), 178 (46).

(10R,11R)-10,11-Dimethyl-DBCH (24).

From 124 mg (0.49 mmol) **16** and 196 mg (1.03 mmol) p-toluenesulfonyl chloride in 3 ml pyridine was prepared the ditosylate as described for **23**. The crude ditosylate was dissolved in 4 ml THF and this solution added dropwise to a suspension of 100 mg $LiAlH_4$ in 20 ml ether. The usual work-up and chromatography (pentane/ ether 100:1) yielded 56 mg of **24** (52%), m.p. 38°C (MeOH). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.4 (d, 6H, two $-CH_3$), 2.9 - 3.2 (m, 2H, two ar$\underline{CH}$-), 4.0 (s, 2H, ar-$\underline{CH_2}$-ar), 6.9 - 7.2 (m, 8H, arom. H). MS: m/z (%) = 222 (76, M^+), 207 (100, $(M-CH_3)^+$), 193 (39), 178 (81), 165 (15).

3-Hydroxy-(4aR,13bR)-1,3,4,4a,9,13b-hexahydro-2H-tribenzo[a,c,e]cyclohepten-2-one (25).

155 mg (6.74 mmol) sodium were melted by heating in 8 ml xylene (under Ar) and then dispersed to sodium sand (vibrator). To the cooled suspension were added 780 mg (7.15 mmol) chlorotrimethylsilane and 505 mg (1.49 mmol) **21** (dissolved in 3 ml xylene) and the mixture was refluxed for 3 h. NaCl was filtered off, the solution was concentrated in vacuo and the residue dissolved in a mixture of 20 ml THF, 10 ml acetic acid and 3 ml 10% aqueous HCl. After stirring 12 h at room temperature 100 ml water were added followed by extraction with ether (50 ml, 3 times). Work-up and chromatographic separation (PE/ethyl acetate 10:1) yielded 224 mg of **25** (54%) and 105 mg (23%) of a ß-ketoester (Dieckmann product), which was identified by its spectral data.

25: m.p. 86°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 2.8 - 2.95 (m, 4H, $-CH_2CO-$ and $-\underline{CH_2}COH-$), 3.25 - 3.4 (m, 1H, ar$\underline{CH}$-), 3.55 - 3.65 (m, 1H, ar$\underline{CH}$-), 3.8 (broad s, 1H, -OH), 3.9 - 4.3 (m, 2H, ar-$\underline{CH_2}$-ar), 4.45 (m, 1H, $-CO-\underline{CH}-OH$), 7.0 - 7.2 (m, 8H, arom. H). IR ($CHCl_3$): 3500, 3000, 2960 - 2860, 1720, 1490, 1450, 1100 cm^{-1}. MS: m/z (%) = 278 (100, M^+), 260 (11, $(M-H_2O)^+$), 234 (28), 205 (92), 191 (85), 179 (95).

ß-ketoester (Dieckmann byproduct): ^{1}H-NMR (400 MHz, $CDCl_3$): 2.7 - 3.1 (m, 2H, $-CH_2-CO-$), 3.8 (s, 3H, $COOCH_3$), 3.8 - 3.9 (m, 2H, ar$\underline{CH}-\underline{CH}$ar), 4.4 (m, 2H, ar-$\underline{CH_2}$ar), 4.6 (m, 1H, $CO-CH-COO-$), 7.0 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2860, 1760, 1730, 1490, 1440, 1260 cm^{-1}. MS: m/z (%) = 306 (24, M^+), 274 (15, $(M-CH_3OH)^+$), 247 (100), 218 (13), 203 (29).

(4aR,13bR)-2,3,4,4a,9,13b-Hexahydro-1H-tribenzo[a,c,e]cycloheptene (26).

To a mixture of 224 mg (0.8 mmol) **25**, 300 mg tin powder and 2 ml acetic acid were added 2 ml conc. HCl. After stirring 30 min. at 80°C another portion of 2 ml conc. HCl was added and stirring was continued for 1 h (80°C). The cooled mixture was poured into 80 ml water, followed by extraction with ether (50 ml, 3 times). Work-up yielded 180 mg crude ketone, which was reduced as follows. A mixture of 180 mg ketone, 400 mg KOH, and 1 ml hydrazine in 5 ml triethyleneglycol was heated at 160°C for 3 h. The cooled mixture was poured into 200 ml water, followed by extraction with ether (50 ml, 3 times). Work-up and chromatography (pentane/ ether 60:1) yielded 101 mg of **26** (total yield 51%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.3 - 2.7 (m, 8H, $-(CH_2)_4-$), 3.0 (m, 2H, two ar$\underline{CH}$-), 4.05 (s, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.25 (m, 8H, arom. H). MS: m/z (%) = 248 (47, M^+), 246 (19), 205 (25, $(M-C_3H_7)^+$), 191 (44), 179 (100).

(5aR,14bR)-5,5a,10,14b-Tetrahydro-1H-dibenzo[3,4;6,7]cyclohepta[1,2-e][1,3,2]dioxathiepine-3-oxide (cyclic sulfite of **16**) (27).

To a solution of 103 mg (0.41 mmol) **16** and 55 mg (0.46 mmol) thionyl chloride in 1 ml CH_2Cl_2 were added 0.5 ml triethylamine and the mixture was stirred for 10 min. at room temperature. It was diluted with 20 ml CH_2Cl_2, washed with water and worked up. Chromatography (PE/ethyl acetate 10:1) gave 114 mg of **27** (94%), m.p. 144°C (PE/ethyl acetate). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.4 - 4.1 (m, 6H, two ar$\underline{CH}\underline{CH_2}$), 4.3 - 4.5 (m, 2H, ar-$\underline{CH_2}$-ar), 7.0 - 7.3 (m, 8H, arom. H). IR: 3000, 2960 - 2860, 1490, 1460, 1190, 980 cm^{-1}. MS: m/z (%) = 300 (8, M^+), 235 (4, $(M-HSO_2)^+$), 205 (100), 191 (58), 178 (44).

(5aR,14bR)-5,5a,10,14b-Tetrahydro-1H-dibenzo[3,4;6,7]cyclohepta[1,2-e][1,3,2]dioxaphosphepine-3-oic acid (cyclic phosphate of **16**) (28).

To a solution of 122 mg (0.48 mmol) **16** and 106 mg (0.67 mmol) $POCl_3$ in 1 ml CH_2Cl_2 were added 120 mg (1.19 mmol) triethylamine. After stirring 30 min. at room temperature it was diluted with 20 ml CH_2Cl_2, washed with water and brought to dryness in vacuo. The residue was refluxed with 30 ml 2% aqueous Na_2CO_3 for 2 h. After cooling the solution was washed with 30 ml CH_2Cl_2 2 times and

the water phase acidified with 10% aqueous HCl. The precipitated acid was filtered off, dried in vacuo and crystallized from ethanol/benzene: 118 mg of **28** (78%), m.p. 226°C (decomposition). IR (KBr): 3010, 2960 - 2900, 2700 - 2500, 1490, 1450, 1240 (PO), 1010 cm^{-1}. MS: 316 (2, M^+), 236 (8, $(M-HPO_3)^+$), 218 (44), 202 (100), 192 (36), 178 (63). Found: P, 9.60%. $C_{17}H_{17}O_4P$ requires P, 9.79%.

(5aR,14bR)-3,3-Dimethyl-5,5a,10,14b-tetrahydro-1H-dibenzo[3,4;6,7]cyclohepta[1,2-e][1,3]dioxepine (isopropylidene acetal of **16**) (**29**).

A mixture of 155 mg (0.61 mmol) **16**, 0.2 ml 2.2-dimethoxypropane and 5 mg p-toluenesulfonic acid in 2 ml benzene was refluxed for 5 min., then evaporated in vacuo and chromatographed (PE/ethyl acetate 10:1): 155 mg of **29** (86%). M.p. 55°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.4 (s, 6H, two $-CH_3$), 3.2 - 3.4 (m, 2H, two arC<u>H</u>-), 3.9 - 4.3 (m, 4H, two $C\underline{H}_2O$), 4.0 (s, 2H, ar-$C\underline{H}_2$-ar), 6.9 - 7.1 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2950 - 2890, 1495, 1460, 1380, 1100 cm^{-1}. MS: m/z (%) = 294 (0.5, M^+), 264 (13, $(M-CH_2O)^+$), 206 (100), 178 (91).

Methyl (10R,11R)-10-carboxy-DBCH-5-one-11-carboxylate (**30**).

To 2.51 g (8.54 mmol) **49** in 35 ml acetone were added 12 ml Jones reagent and the mixture was stirred at room temperature for 16 h. After addition of 6 ml Jones reagent stirring was continued for another 12 h, ethanol was added and the solution was concentrated in vacuo. The suspension of the residue in 50 ml of 5% aqueous HCl was then extracted with ether (50 ml, 3 times). Work-up and chromatography (PE/ethyl acetate 2:1, 1% acetic acid) yielded 2.1 g of **30** (80%), m.p. 194°C (PE/acetone). $[\alpha]_D^{25}$ = +344 (c = 2, dioxane). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.4 (s, 3H, $-OCH_3$), 4.8 (s, 2H, arC<u>H</u>-COO), 7.1 - 7.6 (m, 6H, arom. H), 7.9 - 8.2 (m, 3H, 2 arom. H and COOH). IR (KBr): 3500 - 2800 (OH), 1735 (CO), 1630, 1600, 1440, 1300 cm^{-1}. MS: m/z (%) = 310 (8, M^+), 266 (75, $(M-CO_2)^+$), 251 (45), 233 (35), 207 (55), 178 (100).

Dimethyl (10R,11R)-DBCH-5-one-10,11-dicarboxylate (**31**).

1.49 g **30** were esterified with ethereal diazomethane as usual. Work-up gave **31** in quantitative yield. M.p. 110°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.4 (s, 6H, two $-OCH_3$), 4.8 (s, 2H, two arC<u>H</u>-COO), 7.0 - 7.6 (m, 6H, arom. H), 8.0 - 8.3 (m, 2H, arom. H). IR ($CHCl_3$): 3040 - 2950, 1730, 1640, 1590, 1430, 1290 cm^{-1}. MS: m/z (%) = 324 (25, M^+), 292 (60, $(M-CH_3OH)^+$), 265 (100), 233 (73), 205 (64), 178 (94). UV (CH_3CN): λ_{max} (ε) = 345 (350), 266.5 nm (14530).

(10R,11R)-10-Methoxycarbonyl-DBCH-5-one-11-((1R)-1-phenylethyl)-carboxamide (**32**).

A solution of 200 mg (0.65 mmol) **30** and 78 mg (0.65 mmol) R(+)-phenylethylamine in 1 ml CH_2Cl_2 was cooled to 0°C and then 133 mg (0.67 mmol) DCC were added. After stirring for 12 h at room temperature 20 ml CH_2Cl_2 were added followed by work-up. Chromatography (PE/ethyl acetate 3:1) gave 178 mg of **32** (67%), m.p. 221°C (pentane/CH_2Cl_2). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.2 (d, 3H, $-CH_3$), 3.45 (s, 3H, $-OCH_3$), 4.75 (m, 2H, two arC<u>H</u>-), 4.8 - 5.0 (m, 1H, NCH), 5.3 (m, 1H, NH), 6.5 -6.7 (m, 2H, arom. H), 7.0 - 7.7 (m, 9H, arom. H), 7.9 - 8.4 (m, 2H, arom. H). IR ($CHCl_3$): 3420 (NH), 3010, 1740 (ester), 1660 (CO, amide), 1600, 1510, 1300 cm^{-1}. MS: m/z (%) = 413 (19, M^+), 381 (2), 266 (48), 207 (50), 178 (29), 105 (100).

Nitration of **31** to **33**, **34**, and **35**.

1.557 g (5.02 mmol) **31** were dissolved in 18 ml 95% aqueous HNO_3 at 0°C. The mixture was heated slowly (20 min.) to 50°C. After stirring 5 min. at 50°C the reaction mixture was poured onto 300 g ice followed by extraction with CH_2Cl_2 (80 ml, 2 times). Work-up and chromatographic separation (PE/acetone/ethyl acetate 7:1:2) yielded 187 mg of **33** (9%), 378 mg of **34** (18%) and 504 mg of **35** (24%).

33: Dimethyl 1,6-dinitro-DBCH-5-one-10,11-dicarboxylate.

M.p. 147°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.45 (s, 3H, $COOCH_3$), 3.55 (s, 3H, $COOCH_3$), 4.75 and 5.4 (AB-system, 2H, two arC<u>H</u>-, J = 5 Hz), 7.5 - 7.7 (m, 3H, H(3), H(8), and H(9)), 7.95 (m, 1H, H(4)), 8.15 - 8.3 (m, 2H, H(2), and H(7)). IR ($CHCl_3$): 1745, 1535, 1350 cm^{-1}. MS: m/z (%) = 414 (19, M^+), 382 (60), 355 (100), 323 (48), 59 (91).

34: Dimethyl 1,7-dinitro-DBCH-5-one-10,11-dicarboxylate.

M.p. 159°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.5 (s, 3H, $COOCH_3$), 3.55 (s, 3H, $COOCH_3$), 4.8 - 5.0 (AB-system, 2H, two arC<u>H</u>-, J = 5.3 Hz), 7.5 - 7.65 (m, 3H, H(3), H(4), and H(9)), 7.9 (m, 1H, H(2)), 8.5 (m, 1H, H(8)), 8.85 (m, 1H, H(6)). IR ($CHCl_3$): 1745 (CO), 1535 (as. NO_2), 1350 (s. NO_2)

cm^{-1}. MS: m/z (%) = 414 (9, M^+), 382 (22), 355 (42), 323 (29), 59 (100).

35: Dimethyl 3,7-dinitro-DBCH-5-one-10,11-dicarboxylate.

M.p. 207°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.45 (s, 6H, two $COOCH_3$), 4.9 (s, 2H, two arCH-), 7.5 (m, 2H, H(1) and H(9)), 8.35 (m, 2H, H(2) and H(8)), 9.0 (m, 2H, H(4) and H(6)). IR ($CHCl_3$): 1745, 1535, 1350 cm^{-1}. MS: m/z (%) = 414 (16, M^+), 382 (53), 355 (71), 323 (38), 59 (100).

(10R,11R)-10,11-Bismethoxymethyl-DBCH-5-one (36).

A mixture of 1.34 g (4.75 mmol) **18** and 2.9 g $Mg(NO_3)_2.6\,H_2O$ in 15 ml water was warmed up to 60°C. To the stirred mixture 1.46 g (9.24 mmol) $KMnO_4$ were added in small portions and the temperature was kept at 60°C for 3 h. After cooling to room temperature a mixture of conc. aqueous $NaHSO_3$ and 5% aqueous HCl was added until the precipitated MnO_2 had dissolved, then the solution was extracted with 60 ml CH_2Cl_2 (3 times). Work-up followed by chromatography (PE/ethyl acetate 20:1) yielded 1.37 g of **36** (97%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.1 (s, 6H, two $-OCH_3$), 3.2 - 3.8 (m, 6H, two arCH-CH_2), 7.2 - 7.6 (m, 6H, arom. H), 7.95 - 8.15 (m, 2H, arom. H). IR ($CHCl_3$): 3000, 2940 - 2840, 1650 (CO), 1600, 1450, 1300, 1110 cm^{-1}. MS: m/z (%)= 296 (2, M^+), 264 (14, $(M-CH_3OH)^+$), 251 (9), 220 (26), 193 (18). UV (CH_3CN): λ_{max} (ε) = 345 (430), 267 nm (13920).

Nitration of 36 to 37, 38, and 39.

2.05 g (6.93 mmol) **36** were nitrated as described for **31**. Chromatographic separation (PE/ethyl acetate/acetone 20:4:1) gave 584 mg of **37** (22%), 1.11g of **38** (42%), and 312 mg of **39** (11%).

37: (10R,11R)-1,7-Dinitro-10,11-bismethoxymethyl-DBCH-5-one.

M.p. 92°C (MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 2.9 and 3.3 (m, 2H, CH_2O), 3.05 (s, 3H, $-OCH_3$), 3.1 (s, 3H, $-OCH_3$), 3.5 and 3.7 (m, 2H, CH_2O), 3.8 (m, 1H, arCH-), 4.1 (m, 1H arCH-), 7.5 (m, 2H, H(3) and H(9)), 7.9 (m, 1H, H(4)), 8.05 (m, 1H, H(2)), 8.3 (m, 1H, H(8)), 9.05 (m, 1H, H(6)). IR ($CHCl_3$): 3010, 2940 - 2840, 1660, 1610, 1530, 1350 cm^{-1}. MS: m/z (%) = 280 (2), 252 (1), 208 (6), 45 (100). UV (CH_3CN): λ_{max} (ε) = 337 (720, sh), 249 nm (26150).

38: (10R,11R)-3,7-Dinitro-10,11-bismethoxymethyl-DBCH-5-one.

M.p. 186°C (MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.1 (s, 6H, two $-OCH_3$) 3.2 - 3.45 (m, 4H, two CH_2O), 3.8 (m, 2H, two arCH-), 7.55 (m, 2H, H(1) and H(9)), 8.3 (m, 2H, H(2) and H(8)), 8.95 (d, 2H, H(4) and H(6)). IR ($CHCl_3$): 3020, 2940 - 2840, 1660, 1610, 1530, 1350 cm^{-1}. MS: m/z (%) = 280 (27), 250 (2), 204 (2), 45 (100). UV (CH_3CN): λ_{max} (ε) = 347 (970, sh), 257 nm (35850). Found: N, 7.12%. $C_{19}H_{18}O_7N_2$ requires N, 7.25%.

39: (10R,11R)-3,6-Dinitro-10,11-bismethoxymethyl-DBCH-5-one.

M.p. 89°C (MeOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.05 and 3.35 (m, 2H, CH_2O), 3.1 (s, 3H, $-OCH_3$), 3.15 (s, 3H, $-OCH_3$), 3.5 (m, 2H, CH_2O), 3.8 (m, 2H, two arCH-), 7.55 (m, 3H, H(1), H(8), and H(9)), 7.8 (m, 1H, H(7)), 8.3 (m, 1H, H(2)), 8.8 (m, 1H, H(4)). IR ($CHCl_3$): 3010, 2940 - 2840, 1675, 1610, 1530, 1350 cm^{-1}. MS: m/z (%) = 280 (36), 250 (3), 204 (3), 45 (100). UV (CH_3CN): λ_{max} (ε) = 345 (1150, sh), 245 nm (22490).

(10R,11R)-10,11-Bismethoxymethyl-5-hydroxy-DBCH (40).

To a suspension of 100 mg (2.5 mmol) $LiAlH_4$ in 10 ml ether were added 553 mg (1.868 mmol) of **36**, dissolved in 5 ml ether and this was stirred at room temperature for 10 min. After cooling to 0°C water was added and the precipitate dissolved in 10% aqueous NH_4Cl. General work-up and chromatography (PE/acetone 10:1) gave 538 mg of **40** (97%), m.p. 89°C (ether/pentane). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6 (s, 1H, OH), 3.2 (s, 3H, $-OCH_3$), 3.3 (s, 3H, $-OCH_3$), 3.3 - 4.1 (m, 6H, two ar-CH-CH_2), 6.9 (d, 1H, ar_2CH-O), 7.1 - 7.5 (m, 8H, arom. H). IR ($CHCl_3$): 3600 (OH), 3500 - 3300 (OH), 3000, 2940 - 2840, 1480, 1450, 1120 cm^{-1}. MS: m/z (%) = 298 (1, M^+), 280 (1, $(M-H_2O)^+$), 266 (9), 235 (21), 221 (53), 204 (71), 191 (100), 178 (46).

(10R,11R)-10,11-Bismethoxymethyl-5-hydroxy-5-methyl-DBCH (41).

To a methyl Grignard solution prepared from 250 mg (10.4 mmol) Mg and 1.48 g (10.4 mmol) MeI in 15 ml ether were added 769 mg (2.6 mmol) **36** (dissolved in 5 ml ether). It was stirred at room temperature for 10 min. and then refluxed for a short moment. After adding 10% aqueous NH_4Cl it was extracted with ether and worked up. Purification by chromatography (PE/ethyl acetate 8:1) yielded 706 mg of **41** (87%), m.p. 74°C (ether/pentane). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.9 (s, 3H, $-CH_3$),

3.1 (s, 3H, $-OCH_3$), 3.0 - 4.0 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 3.3 (s, 3H, $-OCH_3$), 7.0 - 7.5 (m, 6H, arom. H), 7.7 - 7.9 (m, 2H, arom. H). IR ($CHCl_3$): 3590 (OH), 3500 - 3300 (OH), 1490, 1450, 1110 cm^{-1}. MS: m/z (%) = 294 (18, $(M-H_2O)^+$), 249 (48), 205 (56), 178 (25).

(10R,11R)-10,11-Bismethoxymethyl-5-methyleno-DBCH (42).

To a cooled solution (0°C) of 440 mg (1.41 mmol) **41** in 10 ml pyridine are added 2 ml $SOCl_2$. After stirring 10 min. at 0°C the reaction mixture was poured onto ice (100 g), acidified with HCl and extracted with CH_2Cl_2 (50 ml, 2 times). General work-up and chromatography (PE/ethyl acetate 15:1) yielded 390 mg of **42** (94%), m.p. 65°C (pentane/ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.2 (s, 6H, two $-OCH_3$), 3.3 - 4.7 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 5.4 (s, 2H, $=CH_2$), 7.1 - 7.5 (m, 8H, arom. H). IR ($CHCl_3$): 3070 - 3010, 2940 - 2840, 1490, 1195, 1115 cm^{-1}. MS: m/z (%) = 294 (4, M^+), 262 (33), 249 (7), 217 (31), 202 (19), 191 (81).

(10R,11R)-10,11-Bismethoxymethyl-3,7-diamino-DBCH-5-one (43).

To a mixture of 870 mg (2.25 mmol) **38** in 30 ml acetic acid and 4 ml conc. HCl were added in small portions 6 g $SnCl_2$. 2 H_2O. After stirring for 30 min. at 80°C the solution was cooled to 0°C and 20 % aqueous KOH was added until pH 10 was reached. Extraction with 80 ml CH_2Cl_2 (3 times), work-up and chromatography (CH_2Cl_2/ethanol 20:1, 0.5% triethylamine) gave 654 mg of **43** (89%), m.p. 58°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.1 (s, 6H, two $-OCH_3$), 3.1 - 3.5 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 3.9 (s, 4H, two $-NH_2$), 6.5 - 7.3 (m, 6H, arom. H). IR ($CHCl_3$): 3460, 3400 (NH_2), 3010, 2940 - 2840, 1625, 1500 cm^{-1}. MS: m/z (%) = 326 (18, M^+), 294 (8), 281 (9), 249 (100), 236 (24), 223 (17). UV (CH_3CN): $\lambda_{max}(\varepsilon)$ = 350 (760), 243 nm (42900).

(10R,11R)-3,7-Diacetamido-10,11-bismethoxymethyl-DBCH-5-one (44).

A mixture of 24 mg (0.07 mmol) **43**, 0.2 ml acetic anhydride and 0.1 ml pyridine in 0.5 ml dioxane was stirred at room temperature for 30 min.. The solvent was evaporated in vacuo and the residue chromatographed (CH_2Cl_2/ethanol 20:1): 28 mg of **44** (96%), m.p. 113 - 114°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 2.3 (s, 6H, two $COCH_3$), 3.2 (s, 6H, two $-OCH_3$), 3.3 - 3.7 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 7.3 - 7.5 (m, 4H, arom. H), 7.9 (m, 2H, arom. H), 8.05 (broad s, 2H, two -NHCO-). IR ($CHCl_3$): 3440, 3320, 3000, 2930 - 2830, 1680 (CO), 1600, 1530, 1310, 1100 cm^{-1}. MS: m/z (%) = 410 (8, M^+), 378 (31), 335 (59), 307 (17), 291 (60). UV (CH_3CN): λ_{max} (ε) = 323 (3190), 246 nm (48500).

(10R,11R)-10,11-Bismethoxymethyl-3,7-diamino-DBCH (45).

To a suspension of 300 mg (7.69 mmol) $LiAlH_4$ in 40 ml ether was added dropwise a solution of 1.025 g $AlCl_3$ (7.69 mmol) in 20 ml ether. After stirring 10 min. at room temperature 312 mg (0.96 mmol) **43** (dissolved in 8 ml THF) were added and the reaction mixture was refluxed for 2 h. To the cooled mixture was added 20% aqueous NaOH until the ether phase became clear. The collected precipitate was refluxed 3 times with a mixture of 50 ml CH_2Cl_2 and 10 ml ethanol. These organic phases were combined and worked up. Chromatography (CH_2Cl_2/ethanol 20:1, 0.5% triethylamine) yielded 275 mg of **45** (92%), m.p. 54°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.25 (s, 6H, two $-OCH_3$), 3.2 - 3.6 (m, 10H, two ar$\underline{CH}$-$\underline{CH_2}$ and two NH_2), 3.9 (s, 2H, ar-$\underline{CH_2}$-ar), 6.35 - 6.55 (m, 4H, arom. H), 6.9 - 7.05 (m, 2H, arom. H). IR ($CHCl_3$): 3450, 3380 (NH_2), 3000, 2920 - 2820, 1620 (NH_2), 1500, 1120 cm^{-1}. MS: m/z (%) = 312 (19, M^+), 280 (10, $(M-CH_3OH)^+$) 267 (75), 235 (75), 222 (100). UV (CH_3CN): λ_{max} (ε) = 296 (4720), 245 nm (21500).

(10R,11R)-10,11-Bismethoxymethyl-3,7-diacetamido-DBCH (46).

62 mg (0.2 mmol) **45** were acetylated as described for **44**. Chromatography (CH_2Cl_2/ethanol 20:1) yielded 74 mg of **46** (94 %), m.p. 102 - 103°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 2.05 (s, 6H, two $COCH_3$), 3.2 - 3.7 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 3.7 (s, 2H, ar-$\underline{CH_2}$-ar), 6.9 - 7.25 (m, 6H, arom. H), 7.6 (s, 2H, two -NHCO-). IR ($CHCl_3$): 3440, 3320, 1680, 1610, 1540, 1130 cm^{-1}. MS: m/z (%) = 396 (8, M^+), 364 (26, $(M-CH_3OH)^+$), 332 (8), 319 (100), 305 (20), 277 (65). UV (CH_3CN): $\lambda_{max}(\varepsilon)$ = 270 (6320), 245 nm (34560).

(10R,11R)-10,11-Bismethoxymethyl-3,7-diacetoxy-DBCH (47).

335 mg (0.93 mmol) **45** were dissolved in a hot mixture (80°C) of 0.4 ml conc. H_2SO_4 and 1.1 ml water. After cooling to room temperature 1 g ice and a solution of 180 mg (2.61 mmol) $NaNO_2$ in 0.5 mol water was added, then the mixture was stirred for 5 min. at 5°C. 1.6 g ice, 1.6 ml water and

20 mg urea (without urea appreciable amounts of dinitroso-diphenols were isolated and characterized by their MS) were added and stirring was continued for 10 min. (5°C). This mixture was added dropwise to a hot suspension (135°C) of 13.8 g Na_2SO_4 in 10 ml conc. H_2SO_4 and 9 ml water. After 10 min. the mixture was cooled, 200 ml water were added and the precipitated diphenol was filtered off. The crude product was refluxed in acetone with charcoal, followed by work-up. Chromatography (chloroform/ ethanol 25:1) yielded 104 mg of a diphenol (31%) as a very unstable compound: MS: m/z (%) = 314 (4, M^+), 299 (10), 282 (22), 237 (64), 211 (26), 45 (100). A mixture of 47 mg (0.15 mmol) diphenol, 5 mg DMAP, 0.1 ml triethylamine, and 0.1 ml acetic anhydride in 0.5 ml dioxane was stirred at room temperature for 10 min., then the solvent was evaporated in vacuo and the residue chromatographed (PE/acetone 7:1). It yielded 56 mg of **47** (93 %) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.25 (s, 6H, two $COCH_3$), 3.25 (s, 6H, two $-OCH_3$), 3.2 - 3.7 (m, 6H, two ar$\underline{CH}$-$\underline{CH_2}$), 4.05 (s, 2H, ar-$\underline{CH_2}$-ar), 6.8 - 7.2 (m, 6H, arom. H). IR ($CHCl_3$): 3000, 2930, 1760 (CO), 1500, 1370, 1200 cm^{-1}. MS: m/z (%) = 398 (0.4, M^+), 366 (11), 324 (36), 279 (40), 237 (28), 45 (100). UV (CH_3CN): λ_{max} (ε) = 277 nm (2590).

5,5'-Bi[(10R,11R)-10,11-bismethoxymethyl-dibenzo[a,d]cycloheptenyl] (**48**).

A suspension of 130 mg (0.84 mmol) $TiCl_3$ and 17 mg (0.47 mmol) $LiAlH_4$ in 3 ml THF was stirred under argon for 30 min. at 0°C. Then 198 mg (0.67 mmol) **36** (dissolved in 1 ml THF) were added and the mixture was refluxed for 3 h. After dilution with 50 ml water and acidification (HCl) the emulsion was extracted with ether (40 ml, 3 times). Work-up and chromatography (PE/ethyl acetate 15:1) yielded 82 mg of **48** (43%), m.p. 207 - 208°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.5 (s, 6H, two $-OCH_3$), 3.6 (s, 6H, two $-OCH_3$), 3.1 - 4.4 (m, 12H, four ar$\underline{CH}$-$\underline{CH_2}$), 6.0 (s, 2H, two $ar_2\underline{CH}$-), 6.8 - 7.5 (m, 16H, arom. H). IR ($CHCl_3$): 3000, 2940 - 2820, 1480, 1450, 1120 cm^{-1}. MS: m/z (%) = 526 (6, M^+), 486 (2), 453 (2), 421 (2), 395 (2), 281 (6), 191 (100).

Methyl (5S,10R,11R)-12-oxo-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-carboxylate (**49**).

A mixture of 2.83 g (9.13 mmol) (-)-**9**, 1.7 g (9.58 mmol) N-bromosuccinimide and 0.1 ml di-tert-butyl peroxide in 80 ml CCl_4 was refluxed for 2 h, then cooled to 0°C and filtered. The organic phase was washed with 50 ml 5% aqueous NaOH (3 times), dried over $MgSO_4$ and evaporated in vacuo. The residue was chromatographed (PE/ethyl acetate 3:1) and yielded 2.5 g of **49** (93%), m.p. 176°C. $[\alpha]_D^{25}$ = +180 (c = 2, dioxane). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.5 (s, 3H, $-OCH_3$) 4.45 (s, 2H, two ar$\underline{CH}$- COO), 5.9 (s, 1H, $ar_2\underline{CH}$-O), 6.9 - 7.2 (m, 8H, arom. H). IR ($CHCl_3$): 3020, 2960, 1750 (CO), 1490, 1360, 1170 cm^{-1}. MS: m/z (%) = 294 (9, M^+), 279 (5), 250 (15, $(M-CO_2)^+$), 191 (100), 149 (31). Found: C, 73.48%; H, 4.82%. $C_{18}H_{14}O_4$ requires C, 73.46%; H, 4.79%.

(5S,10R,11R)-12-Oxo-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-carboxylic acid (**50**).

To a hot solution (50°C) of 86 mg (0.29 mmol) **49** in 5 ml methanol were added 2 ml 20% aqueous KOH. After stirring 1 h at room temperature the solution was concentrated in vacuo, diluted with 20 ml water and washed with CH_2Cl_2 (10 ml, 3 times) followed by acidification (HCl) and extraction with ether (20 ml, 3 times). Work-up and chromatography (PE/acetone 3:1, 1% acetic acid) yielded 70 mg of **50** (85%), m.p. 212 - 213°C (PE/acetone). ^{1}H-NMR (80 MHz, acetone-d6): 4.5 (AB-system, 2H, two ar$\underline{CH}$-COO), 6.25 (s, 1H, $ar_2\underline{CH}$-O), 7.2 - 7.6 (m, 8H, arom. H). IR (KBr): 3600 - 2700 (OH), 1700 (CO), 1480, 1360, 1220 cm^{-1}. MS: m/z (%) = 280 (16, M^+), 236 (24, $(M-CO_2)^+$), 191 (100), 178 (10), 165 (12).

Reaction of **49** with $NaBH_4$ to **51** and **53**.

To a solution of 400 mg (1.36 mmol) **49** in 30 ml methanol were added 362 mg (9.5 mmol) $NaBH_4$ in small portions. After stirring 30 min. at room temperature 5 ml 10% aqueous HCl were added, the solvent was evaporated in vacuo and the suspension of the residue in 50 ml water was extracted with ether (50 ml, 2 times). Chromatographic separation (PE/ethyl acetate 6:1) yielded 174 mg of **51** (48%) and 112 mg of **53** (33%).

51: (5S,10R,11S)-(12-Oxo-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methanol.

M.p. 181°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 2.5 (t, 1H, OH), 3.2 - 3.5 (m, 1H, ar$\underline{CH}$-$\underline{CH_2}$OH), 3.5 - 4.3 (m, 2H, -$\underline{CH_2}$OH), 4.4 (d, 1H, ar$\underline{CH}$COO), 5.95 (s, 1H, $ar_2\underline{CH}$-O), 7.1 - 7.4 (m, 8H, arom. H). IR ($CHCl_3$): 3600 - 3400 (OH), 3020, 1750 (CO), 1490, 1470, 1450, 1370 cm^{-1}. MS: m/z (%) = 266 (0.5,

M^+), 248 (0.5, $(M-H_2O)^+$), 236 (30), 191 (100), 178 (9).

53: (1S,3aS,8S,12bR)-3,3a,8,12b-Tetrahydro-1H-1,8-epoxy-dibenzo[3,4;6,7]cyclohepta[1,2-c]furan.

M.p. 133°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 3.75 (m, 2H, two arC<u>H</u>-), 3.9 - 4.35 (m, 2H, $-OCH_2-$), 5.55 (m, 1H, -OCHO-), 5.6 (s, 1H, $ar_2C\underline{H}-O$), 7.05 - 7.4 (m, 8H, arom. H). ^{13}C-NMR (400 MHz, $CDCl_3$): 46.5 (ar<u>C</u>HCH$_2$O), 47.4 (ar<u>C</u>H-CHOO), 76.5 (arCH<u>C</u>H$_2$O), 79.7 ($ar_2\underline{C}H-O$), 101 (O<u>C</u>HO), arom. C: 123.1, 126.6, 127, 127.2, 127.5, 128.4, 128.7, 130.4, 131.8, 137.9, 140.0, 142.5. IR ($CHCl_3$): 3000, 2960 - 2880, 1490, 1220 cm^{-1}. MS: m/z (%) = 250 (5, M^+), 220 (5, $(M-CH_2O)^+$), 204 (9), 191 (100), 178 (8).

Determination of the stereochemistry at C(11) of 51.

The stereochemistry of **51** was determined by chemical correlation in two ways:

1) The reduction of **51** and **81** with $LiAlH_4$ in ether (cf. **59**) gave identical products (91% from **51**, 85% from **81**), which differed from **59**, viz: (5S,10R,11S)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methanol. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.9 (broad s, 1H, -OH), 3.45 (m, 2H, two arC<u>H</u>-), 3.7 and 4.6 (m, each 1H, $-CH_2O-$), 3.95 - 4.15 (m, 2H, $-\underline{C}H_2OH$), 5.45 (s, 1H, $ar_2C\underline{H}-O$), 7.05 - 7.25 (m, 8H, arom. H). MS: m/z (%) = 252 (4, M^+), 234 (4, $(M-H_2O)^+$), 191 (100), 165 (7). 2) Treatment of **51** with Jones reagent in acetone (cf. **12**) and subsequent methylation of the resulting cis-acid (61%) with ethereal diazomethane gave the cis-ester **81**.

Methyl (5S,10R,11R)-12-thioxo-10,11-dihydro-5H-5,10-thiaethano-dibenzo[a,d]cycloheptene-11-carboxylate (52).

107 mg (0.36 mmol) **49** and 350 mg P_4S_{10} in 8 ml xylene were refluxed for 4 h. The solvent was evaporated in vacuo and the residue taken up with 50 ml 5% aqueous HCl. Extraction with $CHCl_3$ (40 ml, 3 times), work-up and chromatography (PE/ethyl acetate 10:1) yielded 63 mg of **52** (53%). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.6 (s, 3H, $-OCH_3$), 4.65 (d, 1H, arC<u>H</u>-CSS), 5.05 (s, 1H, $ar_2C\underline{H}-S$), 5.25 (d, 1H, arCHCOO), 6.9 - 7.4 (m, 8H, arom. H)- IR ($CHCl_3$): 3000, 1735 (CO), 1490, 1430, 1270 (CS) cm^{-1}. MS: m/z (%) = 326 (24, M^+), 294 (2), 250 (21, $(M-CS_2)^+$), 218 (8), 191 (100). UV (CH_3CN): λ_{max} (ε) = 484 nm (23).

54 and 70 by oxidation of 59.

To a solution of 1.94 g (7.7 mmol) **59** in 80 ml acetone were added dropwise 10 ml Jones reagent (8N). After stirring 30 min. at room temperature ethanol was added and the solvent was evaporated in vacuo. The residue was suspended in 100 ml 5% aqueous HCl followed by extraction with ether (60 ml, 3 times). Work-up and chromatography (PE/ethyl acetate 4:1, 1% acetic acid) yielded 1.15 g of **54** (57%) and 726 mg of **70** (39%).

54: (5R,10R,11R)-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-carboxylic acid.

M.p. 227 - 228°C (benzene). IR (KBr): 3500 - 2700 (OH), 1730 (CO), 1500, 1380, 1240, 1000 cm^{-1}. MS: m/z (%) = 266 (11, M^+), 236 (5), 220 (14), 191 (100), 178 (15).

70: (5R,10R)-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-one.

M.p. 78°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 4.0 - 4.5 (m, 3H, arC<u>H</u>-C<u>H</u>$_2$), 5.7 (s, 1H, $ar_2C\underline{H}-O$), 7.0 - 7.6 (m, 7H, arom. H), 8.0 - 8.2 (m, 1H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 1680 (CO), 1600, 1290 cm^{-1}. MS: m/z (%) = 236 (74, M^+), 208 (100, $(M-CO)^+$), 178 (80), 165 (61), 152 (35). UV (CH_3CH): λ_{max} (ε) = 370 (70), 322 (250), 291 (1570), 222 nm (20900).

Methyl (5R,10R,11R)-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-carboxylate (55).

96 mg (0.36 mmol) **54** were esterified with ethereal diazomethane solution (cf. (-)-**9**). Chromatography (PE/ethyl acetate 10:1) gives 96 mg of **55** (95%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.5 (s, 3H, $-OCH_3$), 3.65 - 3.85 (m, 1H, arC<u>H</u>-), 3.95 - 4.2 (m, 1H, arC<u>H</u>-COO), 4.25 - 4.4 (m, 2H, $-CH_2O-$), 5.45 (s, 1H, $ar_2C\underline{H}-O$), 7.05 - 7.35 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2950 - 2880, 1735, 1495, 1440, 1090 cm^{-1}. MS: m/z (%) = 280 (10, M^+), 250 (5), 221 (30), 191 (100).

(5R,10R,11R)-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-carboxamide (56).

A mixture of 562 mg (2.11 mmol) **54** and 0.5 ml oxalyl chloride (5.7 mmol) was stirred for 12 h at room temperature. After evaporation of the solvent in vacuo the residue was dissolved in dioxane. A dry NH_3-stream was passed through the solution for 30 min. at 0°C and 1 h at room temperature. The solvent was evaporated in vacuo and the residue was suspended in 50 ml water, followed

by extraction with CH_2Cl_2 (50 ml, 3 times). Work-up and chromatography (PE/acetone 2:1) yielded 509 mg of **56** (91%), m.p. 171°C (benzene). ^{1}H-NMR (80 MHz, DMSO-d6): 3.5 - 4.1 (m, 3H, arCH-CH_2), 4.2 (m, 1H, arCH-$CONH_2$), 5.5 (s, 1H, ar_2CH-O), 6.9 - 7.05 (broad s, 2H, $-NH_2$), 7.1 - 7.3 (m, 8H, arom. H). IR (KBr): 3400, 3150, 1680 (CO), 1400, 1080 cm^{-1}. MS: m/z (%) = 265 (8, M^+), 235 (2), 221 (19), 191 (100), 178 (11), 165 (14).

(5R,10R,11R)-10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-((1R)-1-phenylethyl)-carboxamide (**57**).

To a suspension of 266 mg (1.0 mmol) **54** in 5 ml benzene (dry) were added 0.25 ml (2.85 mmol) oxalyl chloride. After stirring 12 h at room temperature the solvent was evaporated in vacuo and the residue dissolved in 3 ml chloroform. 363 mg (3.0 mmol) (+)-phenylethylamine and 0.5 ml triethylamine were added and the solution was refluxed for 2 h. The reaction mixture was poured onto ice, acidified with HCl and extracted with chloroform (40 ml, 3 times). Work-up and chromatography (PE/acetone 8:1) yielded 286 mg of **57** (77%), m.p. 156°C (PE/ethyl acetate). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.25 (d, 3H, $-CH_3$), 3.7 - 3.9 (m, 1H, arCH-), 3.9 - 4.4 (m, 2H, $-CH_2O-$), 4.7 - 5.2 (m, 2H, arCH-CONR and ar-CH-N), 5.45 (s, 1H, ar_2CH-O), 6.5 - 7.4 (m, 13H, arom H). IR ($CHCl_3$): 3420, 3000, 1650, 1490, 1080 cm^{-1}. MS: m/z (%) = 369 (12, M^+), 222 (5, $(M-C_6H_5CHCH_3NCO)^+$), 191 (100), 165 (5), 105 (25, $C_8H_9^+$).

(5R,10R,11R)-10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene-11-((1R,2S)-2-methylamino-1-phenylpropan-1-ol)-carboxamide (**58**).

From 180 mg (0.68 mmol) **54** and 335 mg (-)-ephedrine was prepared the amide **58** as described for **57**. Chromatography (PE/ethyl acetate 3:1) yielded 188 mg of **58** (67%), m.p. 217°C (ethyl acetate/benzene). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.2 (d, 3H, $CHCH_3$), 3.1 (s, 3H, NCH_3), 3.7 (m, 1H, CHN), 3.9 - 4.6 (m, 3H, arCH-CH_2), 4.95 (m, 1H, arCHCONR), 5.4 - 5.5 (m, 2H, arCHOH and ar_2CH-O), 6.3 (d, 1H, OH), 7.05 - 7.5 (m, 13H, arom. H). IR (KBr): 3650 - 3100 (OH), 1640, 1450, 1400 cm^{-1}. MS: m/z (%) = 413 (1, M^+), 395 (1, $(M-H_2O)^+$), 306 (79), 191 (100).

(5S,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methanol (**59**).

To a suspension of 1.0 g $LiAlH_4$ (25.7 mmol) in 60 ml ether were added dropwise 3.92 g (13.33 mmol) **49** (dissolved in 40 ml THF) and this was refluxed for 2 h. The usual work-up (cf. **16**) and crystallization from ether yielded 3.023 g of alcohol **59** (90%), m.p. 173°C.- $[\alpha]_D^{25}$ = +98 (c = 2, dioxane). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6 (s, 1H, OH), 3.1 - 3.4 (m, 2H, two arCH-), 3.5 - 3.9 (m, 2H, CH_2OH), 4.1 - 4.4 (m, 2H, CH_2-OR), 5.4 (s, 1H, ar_2CH-O), 7.1 - 7.4 (m, 8H, arom. H). IR ($CHCl_3$): 3600 (OH), 3450, 3000, 2960 - 2880, 1490, 1460, 1090 cm^{-1}. MS: m/z (%) = 252 (7, M^+), 222 (16, $(M-CH_2O)^+$), 204 (16), 191 (100), 178 (10). Found: C, 80.79%; H, 6.28%. $C_{17}H_{16}O_2$ requires C, 80.93 %; H, 6.39 %.

(5R,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methyl acetate (**60**).

To a solution of 104 mg (0.41 mmol) **59**, 10 mg DMAP and 0.2 ml triethylamine in 2 ml dioxane were added 0.3 ml acetic anhydride. After stirring 30 min. at room temperature the solvent was evaporated in vacuo and the residue chromatographed (PE/ethyl acetate 10:1): 113 mg of **60** (93 %), m.p. 120°C. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.15 (s, 3H, $COCH_3$), 3.4 - 3.6 (m, 2H, two arCH-), 4 - 4.5 (m, 4H, $-CH_2O-$ and $-CH_2$-OAc), 5.35 (s, 1H, ar_2CH-O), 7.1 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 1740 (CO), 1490, 1460, 1380, 1240 cm^{-1}. MS: m/z (%) = 234 (7, $(M-CH_3COOH)^+$), 204 (100), 191 (87), 178 (10).

(5S,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methyl methyl ether (**61**).

To a vigorously stirred mixture of 150 mg (0.6 mmol) **59**, 20 mg tetra-n-butyl-ammonium bromide, 5 ml CH_2Cl_2 and 5 ml 50% aqueous NaOH were added 0.5 ml dimethyl sulfate. After stirring 1 h at room temperature the emulsion was worked up as described for **18**. Chromatography (PE/ethyl acetate 20:1) yielded 124 mg of **61** (78%), m.p. 74 - 75°C (ether/pentane). ^{1}H-NMR (80 MHz/$CDCl_3$): 2.8 - 3.1 (m, 2H, two arCH-), 3.35 (s, 3H, $-OCH_3$), 3.4 - 3.7 (m, 2H,$-OCH_2-$), 3.95 - 4.35 (m, 2H, $-CH_2OMe$), 5.4 (s, 1H, ar_2CH-O), 7.1 - 7.35 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 1490, 1460, 1450, 1095 cm^{-1}. MS: m/z (%) = 266 (8, M^+), 224 (7), 204 (10), 191 (100), 178 (7).

(5R,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methyl fluoride (**62**).

A solution of 285 mg (1.13 mmol) **59** (dissolved in benzene) was stirred in an autoclave with SF_4 for 3 h at 60°C. After the solvent was evaporated in vacuo the residue was suspended in 40 ml 5% aqueous NaOH and extracted with 50 ml CH_2Cl_2. Treatment with charcoal, work-up, and chromatography (PE/ethyl acetate 30:1) gave 172 mg of **62** (60%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.35 - 2.95 (m, 2H, $-CH_2F$), 3.5 - 3.8 (m, 2H, two arC<u>H</u>-), 4.05 - 4.3 (m, 2H, $-CH_2O-$), 5.85 (s, 1H, $ar_2C\underline{H}-O$), 7.1 - 7.5 (m, 8H, arom. H). ^{19}F-NMR (250 MHz, measured with a Bruker WM-250 in $CDCl_3$): -88.9 (m, $-CH_2F$). IR ($CHCl_3$): 3060 - 2940, 1440, 1380, 1090 cm^{-1}. MS: m/z (%) = 254 (35, M^+), 224 (12, $(M-CH_2O)^+$), 191 (28), 178 (100), 165 (12).

(5S,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-nitrile (**63**).

A solution of 320 mg (1.21 mmol) **56** in 3 ml $POCl_3$ was refluxed for 1 h. The cooled reaction mixture was poured onto 100 g ice and the water phase extracted 3 times with 40 ml ether. The organic layer was evaporated in vacuo and the residue was refluxed in 60 ml acetone with charcoal for 30 min.. Work-up and chromatography (PE/ethyl acetate 10:1) yielded 173 mg of **63** (58%) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 3.6 - 3.75 (m, 1H, arC<u>H</u>-CH_2O), 3.9 - 4.35 (m, 2H, $-CH_2O-$), 4.55 (m, 1H, arC<u>H</u>-CN), 5.5 (s, 1H, $ar_2C\underline{H}-O$), 7.1 - 7.7 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 2240 (CN), 1500, 1450, 1090, 1000 cm^{-1}. MS: m/z (%) = 247 (78, M^+), 217 (100), 191 (30), 178 (15).

(5S,10R,11R)-(10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cyclohepten-11-yl)-methane (**64**).

From 255 mg (1.01 mmol) **59** and 210 mg (1.1 mmol) p-toluenesulfonyl chloride was prepared the tosylate as described for **23**. A solution of dried tosylate in 5 ml THF was added dropwise to a suspension of 100 mg $LiAlH_4$ (2.5 mmol) in 20 ml ether. The reaction mixture was refluxed for 1 h, cooled to 0°C, and worked up as usual. Chromatography (PE/ethyl acetate 30:1) yielded 224 mg of **64** (94%), m.p. 88 - 90°C (pentane/ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 1.05 (d, 3H, $-CH_3$), 3.0 - 3.2 (m, 1H, arC<u>H</u>-Me), 3.5 - 3.3 (m, 1H, arC<u>H</u>-CH_2O), 3.9 - 4.4 (m, 2H, $-CH_2O-$), 5.4 (s, 1H, $ar_2C\underline{H}-O$), 7.0 - 7.3 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 1490, 1460, 1100 cm^{-1}. MS: m/z (%) = 206 (73), 191 (100), 178 (29), 165 (19).

Reduction of **70** to **65** and **67**.

To a suspension of 70 mg (1.8 mmol) $LiAlH_4$ in 20 ml THF were added 254 mg (1.08 mmol) **70** (dissolved in 5 ml THF). After refluxing 5 min. water was added to the cooled mixture, followed by acidification (HCl) and extraction (ether). Work-up and chromatographic separation (PE/benzene/ethyl acetate 5:5:1) gave 122 mg of **65** (48%) and 116 mg of **67** (45%).

65: (5R,10R,11R)-11-Hydroxy-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene.

M.p. 147°C (pentane/ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 1.8 (d, 1H, OH), 3.5 (m, 1H, arC<u>H</u>-CH_2), 4.0 - 4.1 (m, 2H, $-CH_2O-$), 4.95 (m, 1H, arC<u>H</u>-OH), 5.45 (m, 1H, $ar_2C\underline{H}-O$), 7.15 - 7.3 (m, 7H, arom. H), 7.55 (m, 1H, arom. H). IR ($CHCl_3$): 3580, 3480, 1495, 1455, 1380, 1090, 1030 cm^{-1}. MS: m/z (%) = 238 (100, M^+), 220 (56, $(M-H_2O)^+$), 209 (45), 191 (69), 179 (83).

67: (5R,10R,11S)-11-Hydroxy-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene.

M.p. 128 - 129°C (pentane/ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 2.4 (broad s, 1H, OH), 3.35 (m, 1H, arC<u>H</u>-CH_2), 3.8 and 4.65 (two m, each 1H, $-CH_2O-$), 5.05 (m, 1H, arC<u>H</u>-OH), 5.45 (s, 1H, $ar_2C\underline{H}-O$), 7.1 - 7.45 (m, 8H, arom. H). IR ($CHCl_3$): 3590, 3400, 3000, 2940 - 2860, 1485, 1090 cm^{-1}. MS: m/z (%) = 238 (77, M^+), 220 (53), 209 (34), 191 (83), 179 (100).

11-Hemiphthalate **66** of **65**.

A mixture of 75 mg (0.32 mmol) **65**, 10 mg DMAP, 53 mg (0.35 mmol) phthalic anhydride and 0.1 ml triethylamine in 0.5 ml dioxane was stirred for 2 h at room temperature. Then 20 ml water were added, the solution was acidified with HCl, followed by extraction with ether (30 ml, 3 times). Work-up and chromatography (PE/acetone 4:1, 1% acetic acid) yielded 108 mg of **66** (89%), m.p. 113 - 115°C. ^{1}H-NMR (80 MHz, acetone-d6): 3.9 - 4.35 (m, 3H, arC<u>H</u>-C<u>H</u>$_2$O-), 5.6 (s, 1H, $ar_2C\underline{H}-O$), 6.5 (d, 1H, arC<u>H</u>-OCOR), 7.2 - 8.0 (m, 12H, arom. H), 10.35 (broad s, 1H, COOH). IR (KBr): 3500 - 2200 (OH), 1700 (CO), 1410, 1270, 1080 cm^{-1}. MS: m/z (%) = 238 (93), 220 (34), 207 (56), 191 (100), 179 (36). UV (CH_3CN): λ_{max} (ϵ) = 273 nm (1030).

11-Hemiphthalate **68** of **67**.

From 71 mg (0.3 mmol) **67** and 49 mg (0.33 mmol) phthalic anhydride was prepared **68** as described for **66**. Chromatography (PE/acetone 4:1, 1% acetic acid) gives 100 mg of **68** (87%), m.p. 108 - 110°C. ^{1}H-NMR (80 MHz, acetone-d6): 3.1 - 3.2 (m, 1H, arCH-), 3.7 - 4.7 (m, 2H, -CH_2O-), 5.6 (s, 1H, ar_2CH-O), 6.45 (m, 1H, arCHOCOR), 7.2 - 8.0 (m, 12H, arom. H), 9.35 (s, broad, 1H, COOH). IR (KBr): 3600 - 2300, 1700, 1400, 1260, 1060 cm^{-1}. MS: m/z (%) = 238 (36), 220 (40), 207 (19), 191 (97), 149 (61), 104 (100). UV (CH_3CN): λ_{max} (ε) = 272 nm (1880).

(5S,10R)-10,11-Dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene (**69**).

A mixture of 240 mg (1.02 mmol) **70**, 100 mg (3.13 mmol) hydrazine and 250 mg KOH in 4 ml triethyleneglycol was first stirred 15 min. at 140°C and then 2 h at 200°C. The cooled reaction mixture was poured into 100 ml water, which was twice extracted with 50 ml ether. Work-up and chromatography (PE/ ethyl acetate 20:1) gives 181 mg of **69** (80%), m.p. 85°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.2 - 3.5 (m, 3H, arCH-CH_2), 3.9 - 4.35 (m, 2H, -CH_2O-), 5.5 (s, 1H, ar_2CH-O), 7.1 - 7.4 (m, 8H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2880, 1500, 1450, 1090, 1010 cm^{-1}. MS: m/z (%) = 222 (30, M^+), 192 (100), 176 (3), 165 (13).

(5R,10R)-11-Methylene-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene (**71**).

From 808 mg (3.21 mmol) **59** and 650 mg (3.40 mmol) p-toluenesulfonyl chloride was prepared the tosylate (cf. **23**). The crude tosylate and 300 mg KOH were added to 6 ml triethyleneglycol and the mixture was heated slowly (1 h) to 200°C. The cooled solution was poured into 150 ml water and extracted with ether (3 times). Work-up and chromatography (PE/ethyl acetate 9:1) gave 630 mg of **71** (84%), m.p. 126 - 127°C (pentane/ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.9 - 4.4 (m, 3H, -CH_2O- and arCH-), 5.25 (s, 1H, ar_2CH-O), 5.55 (d, 2H, =CH_2), 7.1 - 7.4 (m, 7H, arom. H), 7.6 - 7.8 (m, 1H, arom. H). IR ($CHCl_3$): 3000, 2960 - 2860, 1620, 1490, 1080 cm^{-1}. MS: m/z (%) = 234 (5, M^+), 204 (100, $(M-CH_2O)^+$), 178 (7), 165 (3). UV (CH_3CN): λ_{max} (ε) = 298 (560), 260 nm (9460).

Epoxidation of **71** to **72** and **73**.

To a cooled (0°C) solution of 250 mg (1.07 mmol) **71** in 8 ml CH_2Cl_2 260 mg (1.28 mmol) m-chloroperbenzoic acid (85%) was given. After 7 h stirring at room temperature 30 ml CH_2Cl_2 were added. Work-up and chromatography (PE/benzene/ethyl acetate 100:7:2) gave 95 mg of pure **72** (36%) as a colourless oil and 124 mg of a mixture containing **73** (35%) and **70** (12%) as determined from a ^{1}H-NMR-spectrum. Fractional crystallization from ether (3 times) yielded pure **73**.

72: (5R,10R,11R)-5,10-Dihydro-spiro[5,10-oxaethano-dibenzo[a,d]cycloheptene-11,2'-oxirane].

^{1}H-NMR (400 MHz, $CDCl_3$): 2.9 (m, 1H, arCH-), 3.2 (AB-system, 2H, -CH_2O-, epoxide), 4.0 and 4.5 (2m, each 1H, -CH_2O-), 5.6 (s, 1H, ar_2CH-O), 7.0 - 7.35 (m, 8H, arom. H). IR ($CHCl_3$): 3080 - 2880, 1490, 1460 cm^{-1}. MS: m/z (%) = 250 (15, M^+), 220 (80), 191 (97), 190 (93), 189 (100), 178 (24).

73: (5R,10R,11S)-5,10-Dihydro-spiro[5,10-oxaethano-dibenzo[a,d]cycloheptene-11,2'-oxirane].

M.p. 138°C (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): 2.7 (m, 1H, arCH-), 2.95 (AB-system, 2H, -CH_2O-, epoxide), 4 and 4.55 (m, each 1H, -CH_2O-), 5.34 (s, 1H, ar_2CH-O), 6.9 - 7.4 (m, 8H, arom. H). IR ($CHCl_3$): 3080 - 2900, 1490, 1460 cm^{-1}. MS: m/z (%) = 250 (49, M^+), 220 (100), 191 (88), 190 (84), 189 (81), 178 (22).

(5R,10R,11R)-1,11-Bishydroxymethyl-10,11-dihydro-5H-5,10-oxaethano-dibenzo[a,d]cycloheptene (**74**).

To a suspension of 50 mg (1.28 mmol) $LiAlH_4$ in 10 ml ether were added 92 mg (0.33 mmol) **76** dissolved in 2 ml THF. After refluxing for 1 h work-up as for **16** and chromatography (PE/ethyl acetate 4:1) yielded 86 mg of **74** (92%), m.p. 91 - 93°C (pentane/ether). ^{1}H-NMR ($CDCl_3$): 2.2 (broad s, 2H, two OH), 2.9 - 3.5 (m, 2H, arCH-CHar), 3.45 - 4.2 (m, 4H, -CH_2OR and -CH_2OH), 4.6 (m, 2H, arCH$_2$OH), 5.35 (s, 1H, ar_2CH-O), 7.0 - 7.4 (m, 7H, arom. H). IR ($CHCl_3$): 3600, 3550 - 3120, 3000, 2960 - 2870, 1490, 1460, 1080 cm^{-1}. MS: m/z (%) = 264 (10, $(M-H_2O)^+$), 234 (25), 221 (62), 204 (100), 178 (22), 165 (9).

(7R,12R,12aR)-3,7,12,12a-Tetrahydro-1H-7,12-oxaethano-benzo[5,6]cyclohepta[1,2,3-de]isochromene (**75**).

To a solution of 910 mg (3.61 mmol) **73** in 3 ml 1,2-dichloroethane and 3 ml chloromethyl methyl ether were added 500 mg (3.67 mmol) $ZnCl_2$ (dry). After stirring 10 min. at room temperature 50 ml 5% aqueous HCl were added, followed by extraction with CH_2Cl_2 (50 ml, 3 times). Work-up and

chromatography (PE/acetone 10:1) yielded 906 mg of **75** (95%), m.p. 133°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.0 - 3.35 (m, 2H, arC<u>H</u>-C<u>H</u>ar), 3.4 - 4.5 (m, 4H, $-CH_2O-$ and $-C\underline{H}_2-O-CH_2-$ar), 4.7 (m, 2H, ar-$C\underline{H}_2O-$), 5.5 (s, 1H, $ar_2C\underline{H}-O$), 6.8 - 7.25 (m, 7H, arom. H). IR ($CHCl_3$): 3010, 2970, 2880, 1490, 1160, 990 cm^{-1}. MS: m/z (%) = 264 (25, M^+), 234 (14), 204 (34), 178 (5).

(7R,12R,12aR)-1,7,12,12a-Tetrahydro-7,12-oxaethano-benzo[5,6]cyclohepta[1,2,3-de]isochromen-3-one (**76**).

To a cooled solution (0°C) of 370 mg (1.40 mmol) **75** in 30 ml acetone were added in small portions 4 ml Jones reagent (8N) and the mixture was stirred for 30 min.; after adding some ml ethanol the solvent was evaporated in vacuo and the residue suspended in 50 ml water. Extraction with ether (50 ml, 2 times) and general work-up followed by chromatography (PE/ethyl acetate 6:1) gave 351 mg of **76** (90%), m.p. 183°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.1 - 3.7 (m, 2H, arC<u>H</u>-C<u>H</u>ar), 3.9 - 4.2 (m, 2H, $-CH_2O-$), 4.3 - 4.6 (m, 2H, $-CH_2-OCO$), 5.6 (s, 1H, $ar_2C\underline{H}-O$), 6.9 - 7.5 (m, 6H, arom. H), 7.9 (m, 1H, arom. H). IR ($CHCl_3$): 3010, 2960 - 2880, 1730, 1600, 1470, 1400, 1280, 1240 cm^{-1}. MS: m/z (%) = 278 (37, M^+), 248 (100), 218 (30), 190 (44).

(7R,12R,12aR)-1,7,12,12a-Tetrahydro-7,12-oxaethano-benzo[5,6]cyclohepta[1,2,3-de]thioisochromene-3-thione (**77**).

A mixture of 111 mg (0.4 mmol) **76** and 230 mg (0.52 mmol) P_4S_{10} in 8 ml xylene was refluxed for 3 h. The solvent was evaporated in vacuo and the residue suspended in 25 ml 5% aqueous HCl, followed by extraction with $CHCl_3$ (30 ml, 3 times). Work-up and chromatography (PE/ethyl acetate 8:1) gave 75 mg of **77** as a yellow product (61%), m.p. 248°C (PE/ethyl acetate). ^{1}H-NMR ($CDCl_3$): 2.95 - 3.35 (m, 2H, arC<u>H</u>-C<u>H</u>ar), 3.5 - 3.8 (m, 2H, $-CH_2O-$), 3.85 - 4.8 (m, 2H, $-CH_2S-$), 5.25 (s, 1H, $ar_2C\underline{H}-O$), 7.0 - 7.5 (m, 6H, arom. H), 8.2 (m, 1H, arom. H). IR ($CHCl_3$): 3000, 2940, 1470, 1290, 1190, 1180 cm^{-1}. MS: m/z (%) = 310 (69, M^+), 277 (9), 263 (100), 234 (14), 202 (28). UV (CH_3CN): λ_{max} (ε) = 423 (220), 315 nm (14480). Found: S, 20.99 %. $C_{18}H_{14}OS_2^*$ requires S, 20.65 %.

(1'R)-2-(1'-Isochromanyl)-benzoic acid (**78**).

To a vigorously stirred solution of 360 mg (1.53 mmol) **70** in 12 ml dimethyl sulfoxide (0.01 mol-% water) were added in small portions 3.6 g (29.5 mmol) potassium tert.-butylate. After 15 min. the reaction mixture was poured into 150 ml water, acidified with HCl and extracted 2 times with 70 ml ether. The organic phase was evaporated in vacuo and the residue was taken up in 50 ml 10% aqueous KOH. After washing with 40 ml ethyl acetate (2 times) the water phase was acidified (HCl) and extracted with 50 ml ether. General work-up and chromatography (PE/ acetone 4:1, 1% acetic acid) gave 302 mg of **78** (78%), m.p. 145°C (PE/acetone). ^{1}H-NMR (80 MHz, $CDCl_3$): 2.7 - 3.5 (m, 2H, ar$C\underline{H}_2$-), 3.9 - 4.4 (m, 2H, $-OCH_2-$), 6.7 (s, 1H, $ar_2C\underline{H}-O$), 7.1 - 7.6 (m, 7H, arom. H), 8.05 (m, 1H, arom. H), 10.9 (broad s, 1 H, COOH). IR ($CHCl_3$): 3600 - 2400 (OH), 1690, 1600, 1580 cm^{-1}. MS: m/z (%) = 254 (31, M^+), 236 (100, $(M-H_2O)^+$, 207 (50), 178 (44), 133 (79), 105 (39). UV (CH_3CN): λ_{max} (ε) = 272 nm (1730).

(1'R)-2-(1'-Isochromanyl)-benzyl alcohol (**79**).

To a suspension of 100 mg (2.5 mmol) $LiAlH_4$ in 20 ml ether was added dropwise a solution of 288 mg (1.19 mmol) **78** in 5 ml ether and the mixture was refluxed for 1 h. The usual work-up (cf. **16**) and chromatography (PE/ethyl acetate 10:1) yielded 269 mg of **79** (94 %) as a colourless oil. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.7 - 3.4 (m, 3H, ar$C\underline{H}_2$- and OH), 3.8 - 4.4 (m, 2H, $-CH_2O-$), 4.5 (m, 2H, ar$C\underline{H}_2$-OH), 6.0 (s, 1H, $ar_2C\underline{H}-O$), 6.7 - 7.5 (m, 8H, arom. H). IR ($CHCl_3$): 3600 - 3300 (OH), 3000, 2930 - 2850, 1085, 1000 cm^{-1}. MS: m/z (%) = 240 (3, M^+), 221 (100), 194 (28), 178 (25), 165 (21).

cis-DBCH-10,11-dicarboxylic acid anhydride (**80**).

A mixture of 1.584 g (5.62 mmol) **8**, 15 ml acetic anhydride, and 3 ml acetyl chloride was refluxed for 1 h. The solution was cooled to 0°C and the precipitated crystals were filtered off and washed with cold ether. Concentration of the mother liquor in vacuo gave a second crop. Total yield was 1.26 g of **80** (85%), m.p. 263 - 264°C. ^{1}H-NMR (80 MHz, DMSO-d6): 3.7 - 3.8 (AB-system, 2H, ar-CH_2-ar), 5.1 (s, 2H, two arC<u>H</u>-COO), 7.15 - 7.45 (m, 8H, arom. H). IR (KBr): 2900, 2840, 1850 and 1780 cm^{-1} (anhydride). MS: m/z (%) = 264 (23, M^+), 236 (110, $(M-CO)^+$), 192 (100), 165 (14).

Methyl 12-oxo-10,11-dihydro-5H-5r,10-oxaethano-dibenzo[a,d]cycloheptene-11c-carboxylate (**81**).

From 306 mg (0.99 mmol) **3** and 196 mg (1.1 mmol) N-bromosuccinimide in 15 ml CCl_4 was prepared **81** as described for **49**. Crystallization from ether yielded 262 mg of **81** (90%), m.p. 119°C (ether). ^{1}H-NMR (80 MHz, $CDCl_3$): 3.75 (s, 3H, $-OCH_3$), 4.25 (AB-system, 2H, two arC<u>H</u>-), 5.95 (s, 1H, $ar_2C\underline{H}$-O), 7.15 - 7.45 (m, 8H, arom. H). IR ($CHCl_3$) 3020, 1760 (lactone), 1490, 1440, 1290 cm^{-1}. MS: m/z (%) = 294 (6, M^+), 250 (16, $(M-CO_2)^+$), 191 (100), 178 (7), 165 (8). **81** can also be obtained (80 - 90%) from the methyl cis-10-carboxy-DBCH-11-carboxylate by the same procedure. The cis-monomethyl ester was prepared as follows. To a mixture of 4 g (15.15 mmol) **80**, 20 mg DMAP, and 1 ml MeOH in 10 ml dioxane were added 2 ml triethylamine. After stirring 10 min. at room temperature the solvent was evaporated in vacuo and the residue dissolved in 100 ml ether. Washing with 5% aqueous HCl (2 times) and work-up yielded 4.6 g of the cis-monomethylester (98%), m.p. 232 - 233°C (PE/acetone). ^{1}H-NMR (80 MHz, DMSO-d6): 3.6 (s, 3H, $-OCH_3$), 4.1 (AB-system, 2H, ar-CH_2-ar), 4.8 (s, 2H, two arC<u>H</u>-COO), 7.0 - 7.3 (m, 8H, arom. H). IR (KBr): 3500 - 2300 (OH), 1750 (CO), 1710, 1500, 1350. MS: m/z (%) = 296 (3, M^+), 250 (26, $(M-HCOOH)^+$), 191 (100, dibenzotropylium cation), 165 (12). Treatment of the cis-monomethylester with ethereal diazomethane yielded **3** in quantitative yield (by this method it was possible to get **3** in larger scale for the enzymatic experiments).

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