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Synthesis, resolution and determination of energy barriers to rotation of atropisomeric, planar-chiral [*n*]paracyclophanes by dynamic enantioselective gas chromatography and computer simulation

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Abstract

We herein report on the synthesis of substituted carbocyclic [11]paracyclophanes, which are planar-chiral and atropisomeric. Their energy barrier to rotation was determined by dynamic enantioselective gas chromatography on selectively modified cyclodextrins as chiral stationary phases and subsequent computer simulation of the plateau-shaped elution profiles (DGC–CS). The energy barriers are compared with those of analogous dioxa[11]paracyclophanes. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Continuing from our previous studies on rotational energy barriers and the elucidation of substituent effects of axially chiral biphenyls,[1,2] lignans,[3] naphthylazaindoline derivatives[4], and planar-chiral dioxa[11]paracyclophanes,[5] we now report on our investigations of analogous carbocyclic [11]paracyclophanes. Atropisomeric compounds such as planar-chiral cyclophanes or axially chiral biphenyls form a pair of enantiomers due to hindered rotation about a single bond. Depending on the barrier to rotation either conformers or configurationally stable isomers are formed. At room temperature configurational stability requires an energy barrier of approximately 95 kJ/mol.

In recent years we have investigated the stereochemistry and resolution of the enantiomers of several atropisomeric compounds[1,2] by high resolution enantioselective capillary gas chromatography using selectively modified cyclodextrins as chiral stationary phases.[6,7] As a consequence of the competition

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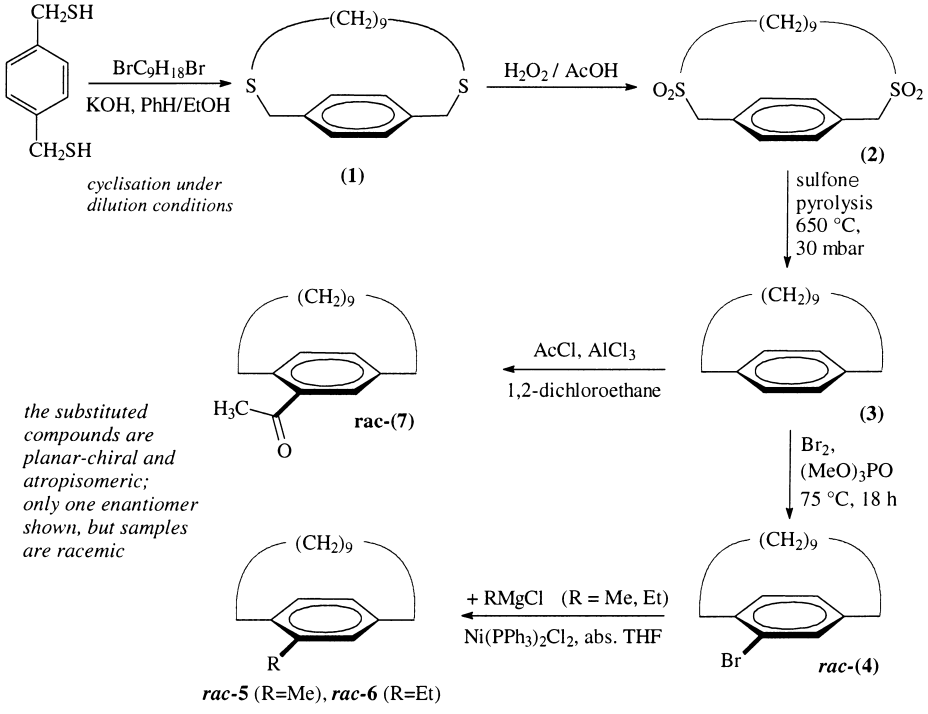
between enantiomeric resolution and simultaneous enantiomerisation (interconversion) during the chromatographic process, coalescence phenomena are observable in the chromatographic elution profiles. Variation of conditions such as temperature, column length and flow rate allows the observation of a range of different elution profiles from base-line separated peaks, over the formation of plateaux between the peaks of both enantiomers, and finally their coalescence and co-elution. Computer simulation of the plateau-shaped elution profiles enables precise and rapid determination of the corresponding energy barriers to rotation without the need for preparative enantiomeric enrichment.[8–10] Recent studies on axially chiral biphenyls gave excellent agreement of the computer simulation results with classical methods.[2] The method is applicable to all chromatographic techniques such as capillary gas chromatography[2,5] (GC), high performance liquid chromatography[4] (HPLC) or subcritical-cryogenic/supercritical fluid chromatography[3] (SFC).

2. Results and discussion

2.1. Synthesis

Synthesis of the atropisomeric [11]paracyclophanes is depicted in Scheme 1.



Scheme 1. Synthesis of atropisomeric [11]paracyclophanes

Preparation of unsubstituted [11]paracyclophane is based on a procedure introduced by Misumi.[11] 1,4-Bis(mercaptomethyl)benzene and 1,9-dibromononane were cyclised in ethanol/benzene with an excess of potassium hydroxide to afford, in good yields (71%), 2,12-dithia[13]paracyclophane, which was subsequently oxidised with hydrogen peroxide in acetic acid to give, in 89% yield, crystalline 2,12-disulfono[13]paracyclophane. The sulfono-groups were extruded from the crude, anhydrous material at 650°C in moderate vacuum (30 mbar) in less than 1 min to yield ca. 40% of the desired carbocyclic

[11]paracyclophane. Substituents were introduced in the aromatic core using the Kumada–Negishi alkylation, by mild bromination and by a rapid low-temperature Friedel–Crafts acetylation.

Only minute amounts of substituted target substances are needed for multiple capillary gas chromatographical studies. Thus, only a few milligrams of each derivative was synthesised. Small samples were isolated by preparative gas chromatography, the purity checked by capillary gas chromatography and the compounds characterised by NMR spectroscopy and mass spectrometric techniques.

2.2. Dynamic chromatography and computer simulation

The modified cyclodextrins heptakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)-β-cyclodextrin and heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin were used as the chiral stationary phase for the enantioselective gas chromatographic investigations.

For precise determination of the barrier of rotation by dynamic gas chromatography combined with computer simulation (DGC–CS) only elution profiles showing plateaux are suitable (Fig. 1). With respect to the energy barrier, compounds within a range of 70–140 kJ/mol can be investigated by DGC–CS, theoretically. But, although gas chromatographic parameters such as column length, flow rate and temperature offer great variability of analytical conditions, the energy barrier and volatility have to be within a suitable range in respect of each other in order to enable the use of this method (Table 1).

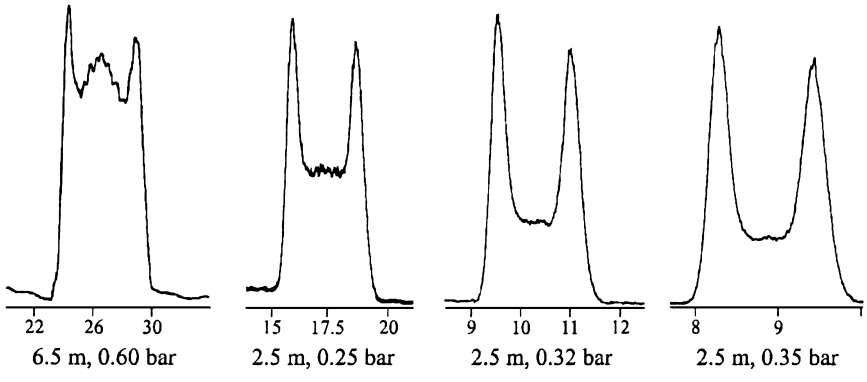


Figure 1. Plateau-shaped elution profiles of 2′-bromo[11]paracyclophane demonstrating the dependence from carrier gas pressure (flow rate) and column length at same temperature. Conditions: heptakis(6-*O*-*tert*-butyl-2,3-di-*O*-methyl)-β-cyclodextrin, 125°C, isothermal

Table 1
Comparison of energy barriers to rotation of atropisomeric dioxa- and carbocyclic [11]paracyclophanes demonstrating the shorter bridge and therefore higher energy barriers of the dioxa-analogues

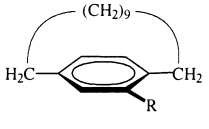
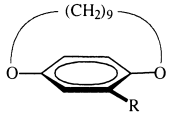
	Energy barriers $\Delta G^{\#}$ [kJ/mol]	
		
2'-substituent	**[11]paracyclophanes**	**dioxa[11]paracyclophanes**
methyl	119.4 at 116.6 °C (**5**)	132.0 at 145.0 °C
ethyl	120.4 at 116.6 °C (**6**)	132.6 at 144.7 °C
bromo	121.1 at 117.1 °C (**4**)	133.1 at 143.7 °C
acetyl	118.6 at 117.1 °C (**7**)	-- / --
carboxymethyl	-- / --	129.2 at 146.3 °C

Table 2
Substituted [11]paracyclophanes, details of dynamic enantioselective gas chromatography and computer simulation experiments

Experiments			Simulation Parameters				Results	
substituent	T	column	t_{dead}	t_{ret1}	t_{ret2}	n_{th}	k	$\Delta G^{\#}$
methyl	105.5	26Me-8	0.30	37.90	48.20	9833	0.02060	118.6
methyl	110.3	26Me-8	0.30	26.85	33.11	10233	0.02850	119.1
methyl	115.1	26Me-8	0.30	19.15	23.10	9012	0.03900	119.6
methyl	120.0	26Me-8	0.30	13.80	16.43	9270	0.05620	120.0
methyl	125.0	26Me-8	0.30	10.18	11.81	14350	0.08430	120.2
methyl	130.2	26Me-8	0.30	7.68	8.73	10700	0.10800	121.0
methyl	116.6	26Me-6	0.20	20.10	24.00	9900	0.04860	119.4
ethyl	111.7	6T-5	0.20	18.00	19.30	12800	0.02300	120.2
ethyl	116.6	6T-5	0.20	12.96	13.82	18400	0.03570	120.4
acetyl	107.6	6T-1.5	0.07	8.90	10.93	1500	0.04400	117.8
acetyl	117.1	6T-1.5	0.07	7.00	8.36	1500	0.06500	118.6
bromo	107.6	6T-2.5	0.10	22.90	27.33	4200	0.01500	121.1
bromo	112.3	6T-2.5	0.10	15.85	18.63	4200	0.01700	121.4
bromo	117.1	6T-2.5	0.10	11.16	12.89	4300	0.02500	121.7
bromo	121.9	6T-2.5	0.10	8.20	9.38	4139	0.03640	122.0
bromo	126.6	6T-2.5	0.10	5.84	6.62	4300	0.06700	122.5
bromo	131.3	6T-2.5	0.10	4.37	4.88	4400	0.09200	123.0
bromo	107.6	6T-1.5	0.07	11.78	14.15	2800	0.01600	120.8

T (°C), temperature of isothermal dynamic GC; t_1 (min), retention time of first eluting enantiomer; t_2 (min), retention time of second enantiomer; t_{dead} (min), dead time of chromatographic system; n_{th} (1), number of theoretical plates; k (min^{-1}), average rate constant of enantiomerisation reaction; $\Delta G^{\#}$ (kJ/mol), energy barrier of enantiomerisation reaction at T.
Columns (stationary phase, length in metres): 6T=heptakis(6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-methyl)-β-cyclodextrin; 26Me=octakis(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin.

We synthesised and gas chromatographically studied substituted [10]-, [11]- and [12]paracyclophanes. The enantiomers of shorter bridged [10]paracyclophanes could be baseline separated and proved to be configurationally stable up to 170°C, so almost no enantiomerisation occurred under gas chromatographic conditions and therefore no plateaux were observed. In contrast, the [12]paracyclophanes are configurationally labile to such a high degree that no enantioseparation could be achieved above 40°C; the lowest temperature possible for our gas chromatographic system. [11]Paracyclophanes exhibit an energy barrier of a suitable dimension, thus showing plateau-shaped elution profiles, and the DGC–CS proved to be a feasible method for determining that barrier. Table 2 summarises all determined enantiomerisation energy barriers for the synthesised derivatives at different temperatures and conditions. Table 1 gives a comparison with analogous dioxa[11]paracyclophanes,[5] a class of compounds with the same number of atoms bridging the aromatic core, but with a slightly shorter bridge due to the closer C–O distances as compared with the C–C-bond length. As expected, the energy barriers to rotation of the dioxa-analogues are decreased by approximately 8–10 kJ/mol compared with the carbocyclic compounds.

The computer simulation is based on the discontinuous plate model, which is applicable to all partition processes and well-known from the rectification theory. Schurig et al. were the first to report on successful simulations using this partition chromatography model.[8–10,12] We have developed a program package optimised for high performance computers,[13] that allows for rapid determination of rate constants and corresponding energy barriers as previously described.[2,5] The agreement of calculated rate constants with classical values is in most cases excellent as recently demonstrated for several atropisomeric biphenyl derivatives[2] without requiring the tedious enantiomeric resolution on a preparative scale. Accuracy of the calculated values is limited by the possible precision of temperature measurement and gas chromatographic conditions. The contribution of the simulation method to the overall error is below

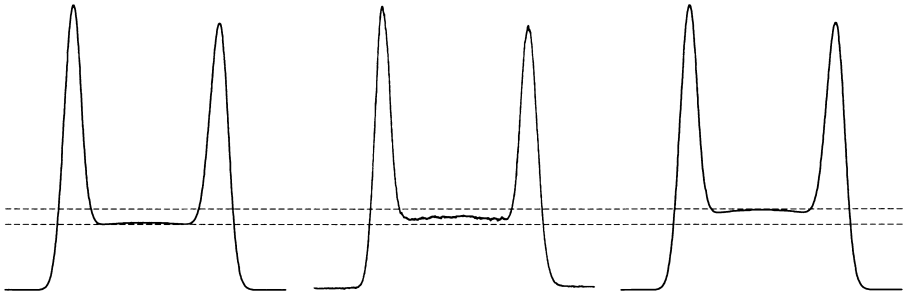


Figure 2. Comparison of simulation (left and right, ±0.2 kJ/mol), and experimental (centre) elution profile

0.15% in most cases. Fig. 2 demonstrates the agreement of experimental and simulated elution profiles, which usually are almost superimposable with each other. One has to be aware of the possible influence of the chiral medium on the energy barrier, i.e. the influence of the chiral stationary phase due to interactions stabilising or destabilising one enantiomer or the rotational intermediate. This is analogous to known solvent effects in classical polarimetric procedures.

3. Conclusion

New planar-chiral, 2′-substituted [11]paracyclophanes were synthesised and their energy barrier to rotation studied by combination of enantioselective gas chromatography and computer simulation of the corresponding elution profiles. This method proved to be a rapid and facile technique for studying interconversion reactions of configurationally labile compounds. Substituent effects were investigated and compared with analogous dioxa[11]paracyclophanes.

4. Experimental

^{1}H NMR spectra: 400 MHz, solvent $CDCl_3$, internal standard $CHCl_3$ (7.26 ppm), Bruker WM 400; MS: VG 70-250 S (VG-Analytical, Manchester UK). Samples were dried by lyophilisation with the freeze dryer Beta A (Christ).

*4.1. Cyclisation to 2,12-dithia[13]paracyclophane **1***

A solution of 500 mg (3.0 mmol) 1,4-bis(mercaptomethyl)benzene and 860 mg (3.0 mmol) of 1,9-dibromononane in 100 mL of benzene was slowly added during 48 h to a refluxing solution of 560 mg (10 mmol) of potassium hydroxide in 200 mL of anhydrous ethanol (dilution conditions). After cooling down to room temperature the reaction mixture was filtered off from insoluble by-products, the solvent removed in vacuo and the crude product purified by liquid chromatography on silica gel with petroleum ether:toluene, 3:2, (R_F 0.34) to afford 610 mg (71%) 2,12-dithia[13]paracyclophane. ^{1}H NMR (400 MHz): δ=0.93 (2 H, m, CH_2-5), 1.04 (4 H, tt, CH_2-4, CH_2-6), 1.18 (4 H, tt, CH_2-3, CH_2-7), 1.33 (4 H, tt, CH_2-2, CH_2-8), 2.39 (4 H, t, J=7.35 Hz, CH_2-1, CH_2-9), 3.67 (4 H, s, CH_2-Ar), 7.28 (4 H, s, arom. H). ^{13}C NMR (100 MHz): δ=26.38 (C-5), 26.65 (C-3, C-7), 27.10 (C-4, C-6), 28.12 (C-2, C-8), 30.70 (C-1, C-9), 36.41 (CH_2−Ar), 128.44 (arom. C_H), 137.72 (arom. C_q). MS (EI, 70 eV) *m/z* (%): 104 (100) [CH_2−C_6H_4−CH_2^+], 294 [M^+].

4.2. Oxidation to 2,12-disulfono[13]paracyclophane **2**

Compound **1** (617 mg, 2.10 mmol) was refluxed for 5 h with 4.6 mL (80 mmol) of glacial acetic acid and 1.39 mL (16 mmol) of 35% hydrogen peroxide solution. After cooling down to room temperature the reaction mixture was left for 1 h at −5°C for crystallisation, then the crude product was filtered off, washed with ice water and lyophilised thoroughly to yield 669 mg (89%) crystalline 2,12-disulfono[13]paracyclophane. ^{1}H NMR (400 MHz): δ=0.88 (2 H, m, CH_2-5), 1.12 (4 H, m, CH_2-4, CH_2-6), 1.32 (4 H, m, CH_2-3, CH_2-7), 1.55 (4 H, m, CH_2-2, CH_2-8), 2.78 (4 H, t, CH_2-1, CH_2-9), 4.30 (4 H, s, CH_2−Ar), 7.55 (4 H, s, arom. H). ^{13}C NMR (100 MHz): δ=20.26, 25. 47, 26.15, 26.78, 50.95, 59.72, 130.47.

4.3. Sulfur dioxide extrusion to [11]paracyclophane **3**

An amount of 100 mg (279 μmol) anhydrous, freshly lyophilised 2,12-disulfono[13]paracyclophane **2** was placed at the bottom of a thick-walled quartz pyrolysis tube and fixed with quartz glass wool. The tube was evacuated to approximately 30 mbar and then placed with the loaded part inside a heating ring, which was able to heat up that part to 650°C in less than a minute. After that period the pyrolysis was finished and the crude product condensed in the cooler part of the tube. It was then dissolved in pentane, purified by liquid chromatography on silica gel with pentane to give 20 to 30 mg (85 to 130 μmol, 31% to 47%), with an average yield of 40% of [11]paracyclophane per run. ^{1}H NMR (400 MHz): δ=0.64 (2 H, m, CH_2-6), 0.82 (8 H, bm, CH_2-4, CH_2-5, CH_2-7, CH_2-8), 1.20 (4 H, m, CH_2-3, CH_2-9), 1.58 (4 H, m, CH_2-2, CH_2-10), 2.59 (4 H, m, CH_2-1, CH_2-11). ^{13}C NMR (100 MHz): δ=25.17 (C-3, C-9), 26.32, 26.98 (C-4, C-5, C-7, C-8), 27.79 (C-6), 28.61 (C-2, C-10), 35.33 (C-1, C-11), 128.60 (arom. C_H), 139.85 (arom. C_q). MS (EI, 70 eV) *m/z* (%): 104 (100) [CH_2−C_6H_4−CH_2^+], 230 (99) [M^+], 105 (42) [CH_3−C_6H_4−CH_2^+], 131 (17), 118 (15), 117 (12). HRMS (EI, 70 eV) *m/z*: 230.2035 (calcd), 230.2028 (found).

4.4. Bromination to 13-bromo[11]paracyclophane **4**

In a 2.5 mL micro reaction vessel 30 mg (130 μmol) [11]paracyclophane **3** was dissolved in a solution of 100 μL (1.95 mmol) bromine (purified by extraction with concentrated sulfuric acid) in 2 mL trimethylphosphate (TMP) and incubated with stirring for 18 h at 75°C. After cooling down to room temperature the reaction mixture was extracted three times with petroleum ether, the combined extracts washed with brine, dried over sodium sulfate and the solvent removed in vacuo. The crude product contained approximately 10% starting material and 2% dibromo[11]paracyclophane and was used without further purification for the Kumada–Negishi alkylations. A small sample was purified by preparative gas chromatography to afford 13-bromo[11]paracyclophane **4** in excellent purity for the DGC investigations and full characterisation. ^{1}H NMR (400 MHz): δ=0.72 (2 H, m, CH_2-6), 0.85 (8 H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8), 1.25 (4 H, m, CH_2-3, CH_2-9), 1.80 (4 H, m, CH_2-2, CH_2-10), 2.45 (1 H, ddd, CH_2-1a), 2.55 (2 H, m, CH_2-11), 3.10 (1 H, ddd, CH_2-1b), 7.05 (1 H, dd, arom. H), 7.10 (1 H, d, arom. H), 7.35 (1 H, d, arom. H). ^{13}C NMR (125 MHz): δ=25.38, 25.81, 26.64, 26.66, 26.72, 27.44, 28.06, 28.13, 28.78, 35.40, 35.55, 128.11, 131.23, 133.26, 139.06, 142.81. MS (EI, 70 eV) *m/z* (%): 184 (100) [CH_2−($C_6H_3{}^{81}Br$)−CH_2^+], 182 (100) [CH_2−($C_6H_3{}^{79}Br$)−CH_2^+], 308 (50) [M^+ (^{79}Br)], 310 (50) [M^+ (^{81}Br)], 131 (48) [M^+−HBr−$(CH_2)_7$], 117 (42) [M^+−HBr−$(CH_2)_8$], 145 (40) [M^+−HBr−$(CH_2)_6$], 229 (18) [M^+−HBr], 230 (4) [M^+−Br]. HRMS (EI, 70 eV) *m/z*: 308.1140 (calcd), 308.1137, 310.1147 (found).

4.5. Kumada–Negishi-coupling to 13-methyl[11]paracyclophane **5**

To a 0.3 mL micro reaction vessel 20 mg (87 μmol) 13-bromo[11]paracyclophane **4** in 280 μL anhydrous tetrahydrofuran was added 37 μL (1.2 equiv.) of a 2.8 mol/L solution of methylmagnesiumchloride, and 2 mg (3 μmol) dichloro-bis(triphenylphosphane)-nickel(II). The sealed vessel was incubated for 24 h at 80°C. After cooling down to room temperature 50 μL of distilled water was added drop-wise, the mixture vigorously stirred for 15 min and the coagulated catalyst filtered off. The solution was dried over sodium sulfate and filtered through a plug of silica gel. The solvent was evaporated in a stream of dry nitrogen, the residue dissolved in dichloromethane and the product isolated by preparative gas chromatography in yields of ca. 1 mg per run with a purity higher than 98% as measured by capillary gas chromatography. The crude product contained 60% of desired 13-methyl[11]paracyclophane, 35% debrominated [11]paracyclophane and 5% of the starting material 13-bromo[11]paracyclophane. ^{1}H NMR (400 MHz): δ=0.70 (2 H, m, CH_2-6), 0.80 (8 H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8), 1.21 (4 H, m, CH_2-3, CH_2-9), 1.57 (4 H, m, CH_2-2, CH_2-9), 2.31 (3 H, s, CH_3), 2.40 (1 H, ddd, J_{gem}=13.5 Hz, J=9.7 Hz, J=4.1 Hz, CH_2-1a), 2.54 (2 H, m, CH_2-11), 2.86 (1 H, ddd, J_{gem}=13.5 Hz, J_1=7.1 Hz, J_2=3.6 Hz, CH_2-1b), 6.93 and 7.02 (2 H, 2 d, J_{ortho}=7.1 Hz, arom. H_{CH-CH}), 6.95 (1 H, s, arom. H_{CMe-CH}). ^{13}C NMR (125 MHz): δ=19.51 (CH_3), 25.57, 25.92, 26.68, 27.17, 27.44, 28.10, 28.11, 28.94, 32.88, 35.76, 126.46 (arom. C_H), 130.01 (arom. C_H), 131.03 (arom. C_H), 135.73 (C_q), 138.14 (C_q), 140.48 (C_q). MS (EI, 70 eV) *m/z* (%): 110 (100) [CH_2−($C_6H_3CH_3$)−CH_2^+], 244 (75) [M^+], 105 (45), 131 (35), 145 (30), 159 (15). HRMS (EI, 70 eV) *m/z*: 244.2191 (calcd), 244.2183 (found).

4.6. Kumada–Negishi-coupling to 13-ethyl[11]paracyclophane **6**

In an analogous procedure to that of methyl-derivative **5**, the reaction of **4** with ethyl magnesium chloride afforded a crude product containing 40% of the desired 13-methyl[11]paracyclophane, 45% debrominated [11]paracyclophane and 5% of the starting material 13-bromo[11]paracyclophane. 2′-Ethyl[11]paracyclophane was isolated by preparative gas chromatography and the purity was confirmed by capillary gas chromatography to be higher than 98%. ^{1}H NMR (400 MHz): δ=0.71 (2 H, m, CH_2-6), 0.80 (8 H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8), 1.18 (4 H, m, CH_2-3, CH_2-9), 1.21 (3 H, t, CH_3), 1.55 (4 H, m, CH_2-2, CH_2-10), 2.42 (1 H, ddd, J=13.2 Hz, J=7.6 Hz, J=3.6 Hz, CH_2-1a), 2.57 (2 H, t, CH_2-11), 2.58 (1 H, m, ethyl–CH_2-a), 2.74 (1 H, m, ethyl−CH_2-b), 2.89 (1 H, ddd, CH_2-1b), 6.94 and 7.03 (2 H, 2 d, J=7.6 Hz, arom. H_{CH-CH}), 6.98 (1 H, s, arom. H_{CH-CEt}). ^{13}C NMR (125 MHz): δ=15.51 (CH_3), 25.49, 25.82, 26.68, 27.39, 28.10, 28.13, 28.18, 28.98, 32.22, 35.86, 126.35 (arom. C_H), 129.26 (arom. C_H), 130.18 (arom. C_H), 137.39 (C_q), 140.59 (C_q), 141.86 (C_q). MS (EI, 70 eV) *m/z* (%): 258 (100) [M^+], 117 (50), 131 (42), 91 (27), 145 (20), 229 (12) [M^+−C_2H_5]. HRMS (EI, 70 eV) *m/z*: 258.2348 (calcd), 230.2328 (found).

4.7. Acetylation to 13-acetyl-[11]paracyclophane **7**

To a solution of 600 μL of 1,2-dichloroethane at −10°C was subsequently added 0.2 g (1.5 mmol) finely powdered aluminium trichloride and 100 μL (1.4 mmol) acetyl chloride. The mixture was stirred for 5 min and then added drop-wise to a −10°C cold solution of 10 mg (43 μmol) [11]paracyclophane in 500 μL 1,2-dichloroethane and stirred for 12 min. After warming up to room temperature 200 μL brine and 300 μL of 2 mol/L hydrochloric acid were added and the mixture extracted three times with carbon tetrachloride. The combined extracts were washed with brine, dried over sodium sulfate, then filtered through silica gel. The solvent was removed in a stream of dry nitrogen, the residue dissolved

in dichloromethane and the product isolated by preparative gas chromatography to afford ca. 1 mg per run with a purity higher than 95% as measured by capillary gas chromatography. The crude product contained varying ratios of the desired product in the range of 40–70% along with the decomposed material. MS (EI, 70 eV) *m/z* (%): 257 (100) [M^+-CH_3], 272 (39) [M^+], 43 (39) [CH_3CO^+], 159 (20) [$M^+-CH_3CO-(CH_2)_5$], 145 (13) 131 (11) [$M^+-CH_3CO-(CH_2)_7$], 117 [$M^+-CH_3CO-(CH_2)_8$], 173 (11) [$M^+-CH_3CO-(CH_2)_4$], 187 (6) [$M^+-CH_3CO-(CH_2)_3$], 215 (4) [$M^+-CH_3CO-(CH_2)$], 229 (6) [M^+-CH_3CO], 201 (3) [$M^+-CH_3CO-(CH_2)_2$]. HRMS (EI, 70 eV) *m/z*: 272.2140 (calcd), 272.2141 (found).

4.8. Preparative gas chromatography for purification

A 20 to 40% solution of the crude [11]paracyclophane derivative in dichloromethane was injected onto a 2.5 m column coated with 10% SE 30 on Chromosorb WAW. A Shimadzu gas chromatograph GC-8A equipped with a thermal conductivity cell and helium was used as the carrier gas. Average amounts of approximately 1 mg could be isolated per run. The purity was in every case confirmed by capillary gas chromatography.

4.9. Dynamic enantioselective gas chromatography

For the enantioselective gas chromatographic investigations, fused silica capillary columns (250 μm inner diameter) coated with a 1:1 (w/w) mixture of the cyclodextrin derivative (cf. Table 1), and polysiloxane OV 1701 were prepared as previously described.[14] Gas chromatography was performed with Carlo Erba Model 2101 gas chromatographs equipped with flame ionisation detectors (FID) and split injectors. Hydrogen was used as the carrier gas.

4.10. Computer simulation

The rate constants of enantiomerisation were determined using computer simulation of elution profiles as described above.[13] Input data are retention times, dead time, number of theoretical plates and the conjectured or known rate constant as start value for the approximation algorithm. Output is the simulated chromatogram in electronic or printed form.

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