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Synthesis of New Chiral Hydrocarbons

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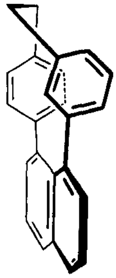
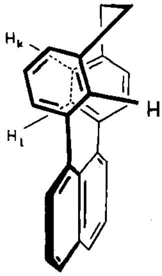
Synthese von neuen chiralen Kohlenwasserstoffen

Unsymmetrisches Anheften einer aliphatischen $(CH_2)_n$-Brücke an ein an sich achirales aromatisches System führt zu starren chiralen Kohlenwasserstoffen des Typs **2**; die Enantiomeren **2a** konnten mit Hilfe von TAPA angereichert werden. Die Racemisierungskinetik wurde polarimetrisch bestimmt: $\Delta G^{\ddagger}_{20} = 93.6\ \mathrm{kJ \cdot mol^{-1}}$.

We describe a concept of designing and building stable chiral hydrocarbons which is based on the idea that bridging symmetrical rigid molecular skeletons, e. g. 1,8-diphenylnaphthalene, unsymmetrically[1] should finally lead to a helical[2] skeleton[3], as is shown by **P**, **M**.

P





M

In contrast to the helicenes and related helical compounds[4], the helical structure[2] here is largely confined to a more or less rigid aliphatic bridge moiety **B**, so that comparative and quantitative investigations of stable aliphatic helices of definite length and pitch are rendered possible. Moreover, with short bridges as in **2a**, the aromatic system can also acquire chirality due to ring distortion. The synthesis of the target molecule **2a** was accomplished by phenyllithium cyclization in tetrahydrofuran of the dibromide **4** which has been obtained by NBS bromination of the hitherto unknown 1-(3-methylphenyl)-8-(4-methylphenyl)naphthalene (**3**).

^1H NMR spectra of **2a** point to a conformationally fixed, strained molecule. The H_i, H_k, and H_l protons, which are situated in the anisotropic region of the opposing phenylene ring, resonate as multiplets extending to the strongly upfield position of 5.7 ppm.

Investigation of the temperature dependence of the proton magnetic resonance spectrum[5] of **2a** leads to the conclusion that this helical structure, the CH_2 protons of which appear as an ABCD pattern between $\delta = 2.1$ and 3.4, is conformationally rigid at ambient temperature. Between 150 °C and the temperature limit of 205 °C (in [d_5]nitrobenzene), the individual signals broaden.

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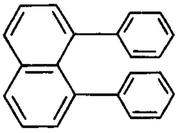
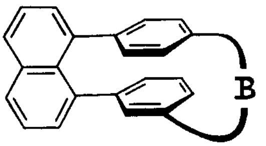
At 205 °C a single still broadened CH_2 absorption is observed. With $T_c \geq 205$ °C and estimating J_{AB} to be 10–15 Hz as well as the unknown $\delta\nu$ to be > 10 Hz, a $\Delta G_c^{\ddagger}$ value of $\gtrsim 102$ kJ · mol^{-1} (24.3 kcal · mol^{-1}) is calculated, indicating enantiomeric separation to be possible.

Since **2a** did not crystallize in enantiomorphic form spontaneously[6], (*S*,*S*)-(+)-2,3-dimethoxy-*N*,*N*,*N'*,*N'*-tetramethyl-1,4-butanediamine[7] as a chiral additive was used in the cyclization of **4** with phenyllithium in tetrahydrofuran, diethyl ether, or pentane in an attempt to induce an enantiomeric excess. However, no optical rotation differing significantly from zero could be obtained. A partial[8a] enantiomeric separation[8b] was finally achieved by chromatography on TAPA-impregnated silica gel[9].

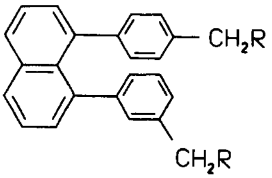


1



2 : B e.g. = $(CH_2)_n$

2a : B = $-CH_2-CH_2-$



3 : R = H

4 : R = Br

With (−)-TAPA, (−)-**2a** was eluted first followed by (+)-**2a**; the inverse order was obtained with (+)-TAPA.

Polarimetric measurements carried out on the enriched (+)- and (−)-fractions at 20, 30, and 40 °C [absolute optical rotation α_D[10] correct to ± 0.100° (CH_2Cl_2)] gave first-order kinetics for interconversion of the M and P[2] form and rate constants [s^{-1}] $k_{20} = 1.30 \cdot 10^{-4}$, $k_{30} = 3.78 \cdot 10^{-4}$, $k_{40} = 1.04 \cdot 10^{-3}$, corresponding to half-lives of 89, 31, and 11 min, respectively. The activation parameters were calculated[11]: $E_a = 80.0$ kJ · mol^{-1}, $\Delta G_{20}^{\ddagger} = 93.6$ kJ · mol^{-1}[12], $\Delta H_{20}^{\ddagger} = 77.6$ kJ · mol^{-1}, $\Delta S_{20}^{\ddagger} = -54.5$ J · mol^{-1} · grad^{-1}.

The relatively small half-lives may well explain why the phenyllithium cyclization in the presence of chiral additives did not lead to any enantiomeric excess, why a continued enrichment by means of TAPA was not successful, and why CD investigations did not give definite conclusions yet.

2a is thus the first enantiomer-separated helical hydrocarbon of such type. The concept may be generalised: Further unsymmetrically bridged „arenicenes" including *o*/*p*- and *o*/*m*-bridged **2** analogues are conceivable starting from different aromatic skeletons, and bridges longer than in **2a** will give information about the dependence of helicity and optical rotation on the bridge structure.

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Experimental Part

1-(3-Methylphenyl)-8-(4-methylphenyl)naphthalene (**3**) was prepared in analogy to the bis(4-methylphenyl) compound[1] by the reaction of bis(3-methylphenyl)lithium cuprate with 1-iodo-8-(4-methylphenyl)naphthalene[1]. Because of the poorer solubility of 3-methylphenyllithium in ether the preparation was run in higher dilution (200 ml solvent per 0.1 mol lithium compound) and under slightly increased temperature (0 °C) and hence in shorter reaction times than described by *House* et al. for the preparation of **1**[13]. Yield 34%; m. p. 68–70.5 °C (methanol).

^{1}H NMR (90 MHz, $CDCl_3/TMS_{int.}$): δ = 2.05 (s, 3H), 2.17 (s, 3H), 6.6–6.9 (m, 8$H_{phenylene}$), 7.3–7.6 (m, 4H), 7.93 (dd, 2H).

$C_{24}H_{20}$ (308.4) Calcd. C 93.46 H 6.54
Found C 93.47 H 6.61 Mol. Weight 308 (MS)

1-[3-(Brommethyl)phenyl]-8-[4-(brommethyl)phenyl]naphthalene (**4**) was obtained as a mixture containing at the most eight byproducts by NBS-bromination of **3** in refluxing CH_2Cl_2. It was used for the subsequent cyclization without purification. A maximum yield of **4** was obtained with a 2.5% excess of NBS [e. g. 2.47 g (8 mmol) **3**, 2.92 g (16.40 mmol) NBS, 150 ml CH_2Cl_2, reaction time 14 h].

[2.0.0](1,3)Benzeno(1,8)naphthalino(1,4)benzenophane (**2a**): Phenyllithium is added dropwise to **4** in THF under vigorous stirring and dilution principle conditions (100 ml of solvent per mmol of **4**). More concentrated solutions led to a drastic decrease in the yield of product. A 1-molar amount of phenyllithium proved to be sufficient; a higher one did not improve the yield. After complete addition the reaction mixture was stirred for another 15 min and then heated to the boiling point of the solvent.

Purification of the worked-up crude oily product by column chromatography (silica gel/n-hexane) yielded a colourless, viscous oil, which quickly crystallized upon standing. Yield 20–30%, based on **3**; m. p. 133.5–135°C (methanol).

^{1}H NMR (90 MHz, $CDCl_3/TMS_{int.}$): δ = 2.1–3.4 (m, 4H), 5.7–7.6 (m, 12H), 7.8–7.9 (m, 2H).

$C_{24}H_{18}$ (306.4) Calcd. C 94.08 H 5.92
Found C 94.09 H 6.04 Mol. Weight 306 (MS)

Enantiomeric separation of **2a**: According to the method of *Klemm* and *Reed*[9b], (+)- or (–)-TAPA[9a] [2-(2,4,5,7-tetranitro-9-fluorenylidenaminooxy)propionic acid, „Newman reagent", $[\alpha]_D^{20}$ = +79.6° (c = 1.27, dioxane) and $[\alpha]_D^{20}$ = –88.2° (c = 1.70, dioxane), resp.] was coated on silica gel (density 10–12%). The enantiomeric separation was carried out at 6°C as described[8a, 9b] with pentane as eluant (column 100 cm × 1.5 cm, addition rate 10 ml/h). The collected fractions (10–20 ml) were cooled rapidly to –78°C, then evaporated to dryness at $\leq$15°C in vacuo and examined polarimetrically (in CH_2Cl_2)[14]. Fractions with identical signs of optical rotation were mixed before the kinetic measurements. The racemate formed did not show any sign of decomposition.

Literature

[1] For achiral, symmetrically bridged aromatic skeletons see: *W. Bieber* and *F. Vögtle*, Angew. Chem. **89**, 199 (1977); Angew. Chem., Int. Ed. Engl. **16**, 175 (1977).

[2] On the helicity of variously twisted short chains of atoms: *J. H. Brewster*, Top. Curr. Chem. 47, 29 (1974); see also: International Union of Pure and Applied Chemistry, Rules For The Nomenclature of Organic Chemistry, Section E: Stereochemistry, Pure Appl. Chem. **45**, 29 (1974).

[3] In the course of our work, *M. Nakazaki, K. Yamamoto* and *Y. Miura*, J. Org. Chem. **43**, 1041 (1978), reported the properties of the triple-bridged [2.2.2](1,2,4)(1,3,5)- and [2.2.2](1,2,4)-(1,2,5)benzenophanes, which show chirality because of one unsymmetrical bridge; no attempts to separate the more labile compounds were mentioned however.

[4] Noncondensed helices with aromatic screw moieties: [4a] *F. Vögtle, M. Atzmüller, W. Wehner*, and *J. Grütze*, Angew. Chem. **89**, 338 (1977); Angew. Chem., Int. Ed. Engl. **16**, 325 (1977). – [4b] *E. Hammerschmidt* and *F. Vögtle*, Angew. Chem. **90**, 293 (1978); Angew. Chem., Int. Ed. Engl. **17**, 268 (1978); Chem. Ber. **112**, 1785 (1979).

[5] See also the conformationally mobile achiral [2.2](1,3)(1,4)benzenophane: *F. Vögtle* and *P. Neumann*, Chimia **26**, 64 (1972).

[6] **2a** crystallizes in the monoclinic space group Ic or $I2/c$ with a = 28.8, b = 8.06, c = 14.1 Å, β = 103° and z = 8. We thank Prof. Dr. *H. Irngartinger*, D-6900 Heidelberg, for undertaking the X-ray analysis.

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[7] *D. Seebach, H.-O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Doerr, N. P. DuPreez, V. Ehrig, W. Langer, Ch. Nuessler, Hoc-An Oei,* and *M. Schmidt,* Helv. Chim. Acta **60**, 301 (1977).

[8] Compare [8a] *M. Haenel* and *H. A. Staab,* Chem. Ber. **106**, 2203 (1973). – [8b] *F. Mikes, G. Boshart,* and *E. Gil-Av,* J. Chem. Soc., Chem. Commun. **1976**, 99.

[9] [9a] *P. Block jr.* and *M. S. Newman,* Org. Synth. **48**, 120 (1968). – [9b] *L. H. Klemm* and *D. Reed,* J. Chromatogr. **3**, 364 (1960).

[10] A specific rotation value $[\alpha]_D$ of the pure enantiomer cannot be given because the degree of separation is unknown.

[11] The calculated values of ΔG^{+}, ΔH^{+}, ΔS^{+} at 20 and 40°C are 93.6 and 94.7 $kJ \cdot mol^{-1}$, 77.6 and 77.4 $kJ \cdot mol^{-1}$, -54.5 and -55.0 $J \cdot grad^{-1} \cdot mol^{-1}$, resp. The small differences lie within the limits of error (for ΔG^{*} estimated to be $\approx \pm 4$ $kJ \cdot mol^{-1}$) of the approximation method.

[12] *H. O. House, W. J. Campbell,* and *M. Gall,* J. Org. Chem. **35**, 1815 (1970), and *R. L. Clough* and *J. D. Roberts,* ibid. **43**, 1328 (1978), found ΔG^{*} for rotation to be 63 – 67 $kJ \cdot mol^{-1}$ in the 1,8-diarylnaphthalene system. *R. L. Clough* and *J. D. Roberts,* J. Am. Chem. Soc. **98**, 1018 (1976), calculated 100 $kJ \cdot mol^{-1}$ for 1,8-bis(2-methylphenyl)naphthalene, in which rotation is hindered by the naphthalene protons in 2-position.

[13] *H. O. House, D. G. Koepsell* and *W. J. Campbell,* J. Org. Chem. **37**, 1003 (1972).

[14] Polarimeter 241 (Perkin-Elmer).

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