Synthesis of a Mesogenic Compound with a Defined Conformation

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Abstract: The synthesis of the bicyclohexyl derivative 2 has been attained in 4 steps by bi-directional elaboration of bicyclohexanone 3. Due to the specifically placed methyl substituents, 2 populates a single conformation at the inter-ring bond, resulting in improved material properties.

Key words: carbocycles, conformation, fluorine, liquid crystals

Increased use of liquid crystal displays in electronic devices led to a constantly growing demand of new liquid crystalline materials with optimal properties, such as high clearing temperature, low rotational viscosity or high dielectric anisotropy (Δε). Recent studies on liquid crystalline compounds of the type 1 demonstrated a remarkable dependence of the dielectric anisotropy of these axially fluorinated bicyclohexyl derivatives on the conformation of the molecular backbone. AM1-calculations indicated that the dielectric anisotropy vanishes when the dipole moments of the C-F bonds point in opposite directions and cancel each other, i.e. if the conformation at the bicyclohexyl bond is trans (Φ = dihedral angle H-C-C-H = 180°), cf. Scheme 1. In conformations with smaller dihedral angles the dipoles reinforce each other: the smaller Φ the more negative will be the dielectric anisotropy Δε. The actual value of Δε is then the population weighted average over the conformer population.

Compound 1 populates two types of conformation: The gauche conformation 1b (58%, calculated Δε = -2.7) and the trans conformation 1a (42%, calculated Δε = -0.4). A Boltzmann distribution over the two conformations 1a and 1b predicts an averaged Δε-value of -1.7, which is slightly lower than the experimentally determined value of Δε = -2.5. Obviously, if the conformer equilibrium can be shifted in the direction of 1b, the compounds should possess larger negative Δε-values. A shift in the conformer population toward 1b could be attained by rational placement of substituents, i.e. by rational conformation design.

We therefore targeted the C2-symmetric compound 2, which has two additional methyl groups compared to compound 1. While maintaining free rotation about the inter-ring bond the two equatorial methyl groups should destabilize both the trans conformation 2a as well as one of the two possible gauche conformations (2c) by two syn-pentane interactions to the point that these arrangements are no longer minima on the rotational energy profile (a comparison of the calculated rotational profiles for 1 and 2 is given in Figure 1). The calculations show for 2 only two minima on the rotational energy profile: 2b (Φ = -60°) and, substantially (+4.9 kcal mol⁻¹) higher, another conformer which reduces syn-pentane interactions by increasing the dihedral angle Φ to 80°. Compound 2 should therefore populate exclusively the strain-free gauche conformation 2b (cf. Scheme 2) which, due to the small dihedral angle at the inter-ring bond should lead to a significantly larger negative Δε-value.
The synthesis of compound 2 originated from 4,4'-dicyclohexanone 3. In a bi-directional approach, 3 was converted to the bis-silylenoether, which was transformed into the bis-enone 4 using the Saegusa protocol. This led to a 1:1 mixture of the meso- and d/l-diastereomers. Subsequent addition of Me₂CuLi introduced the two methyl groups selectively trans to the cyclohexyl substituent furnishing a mixture of meso-5 and d/l-6. The diastereomers were both crystalline compounds. X-ray crystal structure analysis of 5 showed that this is the diastereomer which has the proper relative configuration for the synthesis of 2. Wittig reaction of 5 with pentyldiene-phosphorane led to an E/Z-mixture of the bis-alkene 7. Following earlier precedent, the bis-alkene was converted with HF/pyridine (Olah’s reagent) into the target compound 2, which was recrystallized to diastereomeric purity.

Conformational analysis of the bicyclohexyl derivatives rests on a determination of the 3JH-H coupling constant across the inter-ring bond. In the case of compound 2, this was prevented by severe signal overlap. We therefore turned to conformational analysis of the precursor ketone 5, which should display a similar conformational behavior to that of 2. The SELINCOR technique without proton decoupling permitted the determination of the 3JH-H coupling constant across the inter-ring bond to J = 3.0 Hz. This value documents the predominance of a gauche conformation but does by itself not differentiate between the two possible gauche conformations to 5b and 5c. Since the conformation 5b is the only one free of syn-pentane interactions, the latter is likely the predominant conformation. This is indeed the conformation found in the solid state, as the X-ray crystal structure of 5 shows (Scheme 4).

The high conformational preference found for the ketone 5 should also prevail in the difluoro compound 2, a fact that should be reflected in the dielectric anisotropy of compound 2. With a Δε-value of ~4.2, compound 2 possesses indeed a much improved dielectric anisotropy compared to compound 1.
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References and Notes

(3) The energy profile for the rotation about the inter-ring bond was calculated using the MMFF94 force field. The structures corresponding to the minima were optimized by AM1-calculations and used as input for the calculations of the Δ values.


(9) Bicyclohexyl-2,2′-dione-4,4′-dione (4) n-BuLi (1.53 M in hexane). 67.0 mL, 103 mmol was added at -78 °C into a solution of disobutylamine (15.1 mL, 108 mmol) in THF (150 mL). The mixture was cooled to 0 °C for 10 min, then cooled to -78 °C prior to addition of a solution of the diketone (4.857 g, 25.00 mmol) in THF (20 mL). After stirring for 2.5 h an aqueous ethanolic solution of Pd(OAc)2 (5.980 g, 10.00 mmol) was added. After stirring for 1 h the reaction mixture was filtered over a small pad of celite. After removal of the solvent the residue was extracted with pentane (3 × 70 mL) and successively treated with Pd(OAc)2 (5.980 g, 10.00 mmol) and a solution of the catalyst (0.16 mol/L) in Et2O (10 mL). The mixture was stirred for 1.5 h and then filtered over a short pad of celite. After removal of the solvent the residue was purified by flash chromatography (pentane/tert-butyl methyl ether 1:9) to give dienone (4.384 g, 92%) as a pale yellow solid as a mixture of (R,R,R)- and (R,S,R)-meso-4,4′-butoxydiketone (168 mg, 98%) as a colorless oil. 1H NMR (500 MHz, CDCl3); δ = 1.08-1.04 (m, 6H, J = 6.6 Hz), 1.26 (t, 2H, J = 4.3 Hz, J1 = 13.5 Hz), 1.72-1.78 (m, 2H, J2 = 13.5 Hz, 1.87-1.91 (m, 4H, 2H), 2.14 (t, 2H, J = 13.5 Hz), 2.30 (td, 2H, J1 = 6.1, 13.5 Hz), 2.39-2.43 (m, 4H); 13C NMR (75 MHz, CDCl3); δ = 17.9 (2C), 24.6 (2C), 35.1 (2C), 41.1 (2C), 42.5 (2C), 49.9 (2C), 210.7 (2C); Anal. Calcd for C14H22O2: C 75.63; H 9.97; Found: C 75.50; H 9.88. 6: R, R, R (4-4′)-diphenyl-substituted (pentane/tert-butyl methyl ether 1.1:9) afforded dl-diketone 5 (246 mg, 36%) and meso-diketone 6 (261 mg, 36%) as colorless solids. 6: R, R, R (pentanol/tert-butyl methyl ether 1:1.9) mp: 92 °C; 1H NMR (500 MHz, CDCl3); δ = 1.03 (6H, J = 6.4 Hz), 1.40 (d, 2H, J = 4.3 Hz, J1 = 13.5 Hz), 1.72-1.78 (m, 2H, J2 = 13.5 Hz), 1.72-1.80 (m, 4H, J1 = 13.5 Hz, J2 = 13.5 Hz); 13C NMR (75 MHz, CDCl3); δ = 19.7 (2C), 24.6 (2C), 35.1 (2C), 41.1 (2C), 42.5 (2C), 49.9 (2C), 210.7 (2C); Anal. Calcd for C14H22O2: C 75.63; H 9.97; Found: C 75.50; H 9.88. 6: R, R, R (4-4′)-diphenyl-substituted (pentane/tert-butyl methyl ether 1:1.9) mp: 92 °C; 1H NMR (500 MHz, CDCl3); δ = 0.75 (6H, J = 6.6 Hz, J = 6.6 Hz), 1.20-1.24 (m, 2H, 2H), 1.27 (dd, 2H, J = 4.2, 12.6 Hz), 1.34-1.42 (m, 2H, J1 = 4.5, 14.1 Hz), 2.27-2.31 (m, 2H, J = 4.2, 13.5 Hz), 2.45 (t, 2H, J1 = 6.1, 13.5 Hz); 13C NMR (75 MHz, CDCl3); δ = 21.2 (2C), 28.6 (2C), 34.9 (2C), 40.7 (2C), 44.6 (2C), 49.4 (2C), 211.1 (2C); Anal. Calcd for C14H22O2: C 75.63; H 9.97; Found: C 75.92; H 10.06.


(11) 2,2′-Dimethyl-bicyclohexyl-4,4′-dione (5). Melilithium (1.3 M in Et2O, 155 mL, 20.1 mmol) was added at 0 °C to a suspension of Cul (1.916 g, 10.06 mmol) in Et2O (50 mL). The solution was cooled to -78 °C and of a solution of the diene 4 (598 mg, 3.14 mmol) in Et2O (10 mL) was added dropwise. After warming to 0 °C over 5 h a saturated aqueous NH4Cl solution (50 mL) and concd. aqueous NH4OH (25 mL) were added. The phases were separated and the aqueous phase was extracted with tert-butyl methyl ether (3 × 40 mL). The combined organic phases were washed with brine (10 mL), dried (Na2SO4) and concentrated. Purification by flash chromatography (pentane/tert-butyl methyl ether 1:5:1) afforded dl-diketone 5 (246 mg, 36%) and meso-diketone 6 (261 mg, 36%) as colorless solids. 5: R, R, R (pentanol/tert-butyl methyl ether 1:9) mp: 70 °C; 1H NMR (400 MHz, CDCl3); δ = 0.83 (d, 6H, J = 6.6 Hz), 0.89 (t, 6H, J = 6.6 Hz), 1.01 (dd, 2H, J = 12.5, 13.7 Hz), 1.11-1.19 (m, 2H, J = 2.9, 15.8 Hz), 1.29-1.58 (m, 22H), 1.74-1.93 (m, 6H); 13C NMR (100 MHz, CDCl3); δ = 14.0
(2C), 19.2 (2C), 20.3 (2C), 22.6 (2C), 22.8 (d, 2C, $J = 4.7$ Hz), 28.8 (2C), 32.3 (2C), 35.2 (d, 2C, $J = 22.9$ Hz), 41.1 (d, 2C, $J = 22.8$ Hz), 43.3 (2C), 44.6 (d, 2C, $J = 22.6$ Hz), 96.0 (d, 2C, $J = 167.2$ Hz); $^{19}$F NMR (188 MHz, CDCl$_3$): $\delta = -157.5$; Anal. Calcd for C$_{24}$H$_{44}$F$_2$: C 77.78; H 11.97; Found: C 77.79; H 12.26.


(18) The $\Delta$e-values were determined by linear extrapolation from a 10% w/w solution in the commercially available Merck mixture ZLI-2857 ($T_{NI} = 82.3$ °C, $\Delta \varepsilon = -1.42, \Delta n = 0.0776$) as a standard host.

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