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Alkynyl Expanded Donor–Acceptor Calixarenes: Geometry and Second-Order Nonlinear Optical Properties

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Abstract: A number of wide- and narrow-rimmed functionalized alkynylcalix[4]arenes have been synthesized by Sonogashira coupling. With respect to their optical properties, these donor–acceptor systems are treated as ensembles of covalently linked, electronically independent tolane subchromophores. Linear UV/visible and fluorescence spectroscopic investigations revealed that the charge-transfer character of the electronic transitions in calixarenes, and also the second-order nonlinear optical (NLO) properties depend on the electron-withdrawing nature of the terminal ethynylphenyl substituent (NO_2, CF_3, H). The nitro derivatives display high values of the quadratic hyperpolarizability β. Not only do the (nonlinear) optical properties of the target compounds depend on the number and relative disposition of the subchromophores, but also on the geometry of the calixarenes. In particular, the opening angle of the calixarene cavity can be determined by the substitution pattern of the calixarene scaffold (wide- versus narrow-rim substitution) and the number of the acetylene functions introduced. Both the NLO properties and the conformational issues are conveniently assessed by using hyper-Rayleigh scattering (HRS) in solution, and supported by X-ray crystallography in the solid state.

Keywords: alkynes · calixarenes · conformation analysis · nonlinear optics · Sonogashira coupling

Introduction

Within the field of calixarene-based supramolecular systems,[1] the prospect of having deep cavitands has gained increasing importance over the past years.[2] Enlarged supramolecular scaffolds for molecular recognition of larger guest molecules, the possibility of utilizing large container molecules to carry out chemical reactions in their interior, and the construction of noncovalent assemblies in nanoscale dimensions has, among other incentives, led to an intensification of synthetic efforts to access deep calixarenes by means of covalent synthesis.[3] Among various methods, the palladium-catalyzed Sonogashira cross-coupling of halogenated calixarene precursors with terminal acetylenes has been established as one of the most efficient strategies to achieve this goal.[4] Various research groups have reported alkynylcalixarenes as molecular receptors,[5] building blocks for supramolecular assemblies,[6] coordination compounds,[7] and electro-optical devices.[8] A particularly attractive challenge is the exploitation of the flexibility of the cavitand scaffold for the purpose of transferring molecular movement to an appreciable nanometer scale.[9] Diederich et al. have reported a molecular muscle, a resorcinarene-based device which can perform movement over a distance of 70 Å. This process relies on the expansion and contraction of the flexible, acetylene-expanded cavity of a resorcinarene system.[10] Likewise, the group of Weiss has prepared different pincer-type

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ligands based on a bisalkynylcalix[4]arene platform in which the terminal porphyrin receptor moieties can adjust their intermolecular distance to the steric demands of the respective bifunctional guest molecules.[11] In these types of tweezer molecules, molecular motion can be stimulated by an electrochemical input.[12] Again, the principle of molecular movement is based on the flexibility of the calixarene platform. In both examples, the extension of the cavitand by triple-bond substitution guarantees a controlled, one-dimensional orientation of the molecular movement. In contrast to vinylic or diazo systems, which can undergo *cis–trans* isomerisation, rigid, linear acetylene systems do not possess such additional complications to their conformational freedom.

Another facet of calixarenes of continuing relevance is their application as nonlinear optical chromophores.[13] Guided by the pioneering work of Reinhoudt and Persoons,[14] we have also recently focused our research on organic molecules for second-order nonlinear optics, that is, on the use of alkynyl-substituted calixarenes. In the case of alkynyl-substituted calixarenes, these systems can be considered as an ensemble of independent, dipolar tolane subchromophores held together in a defined, pseudo-rigid conformation. In the case of nonlinear optically-active calixarenes, as well as in the examples outlined above, the determination of the relative orientation of the subunits to each other is a crucial issue. The dipolar and octopolar components that contribute to the overall hyperpolarizability of donor–acceptor (D–A)-substituted calix[4]arenes in their different conformations (cone, partial cone, 1,2-alternate, and 1,3-alternate) have been investigated experimentally and by computational methods.[15] The variation of the interdipolar angle between the aromatic subunits has been assessed employing theoretical calculations.[16] In solution, this important parameter, the opening angle of the calixarene cavity, could only be measured qualitatively by dipolometry and,[17] traditionally, NMR spectroscopy. Depending on the chemical shifts of the methylene bridge ^{13}C NMR signals, the calixarene is described as more or less conical.[18] In a first communication, we have shown that hyper-Rayleigh scattering is a useful tool to determine the interdipolar angle in tetraalkynyl calix[4]arenes in solution.[19] Although X-ray crystallography is an invaluable technique for static structure determination in the solid phase, it is obvious that a reliable solution-based analytical method for the average structure of these highly dynamic systems, the typical medium of study of which is the liquid phase (extraction, self-assembly, molecular recognition, etc.), is highly desirable. In continuation of our previous work, we have designed an elaborate series of second-order NLO-active, expanded calix[4]arenes in which the calixarene platform is substituted on both the upper- or lower-rim by two or four arylethynyl moieties (Figure 1).

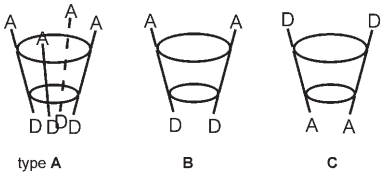


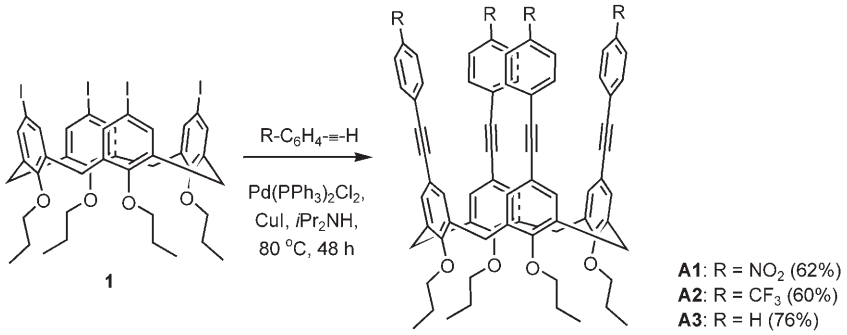
Figure 1. Schematic depiction of different D–A-substituted bis- and tetraalkynylcalix[4]arenes.

The introduction of D–A end groups into the tolane subunits should give rise to a high NLO activity (NLO = nonlinear optical). The different types of calixarenes were chosen to vary the flexibility of the molecular scaffold and, therefore, a variation of the interdipolar angle is expected. Furthermore, this angle, that is, the opening of the calixarene cavity, and also the second-order NLO properties can be determined by hyper-Rayleigh scattering (HRS). The conformation analysis in solution is accompanied by, where possible, a single crystal X-ray structure determination or by molecular modeling calculations.

Results and Discussion

Synthesis: The synthesis of the upper-rim alkynylated compounds **A1**–**A3** was achieved in good yields by fourfold Sonogashira coupling of the tetraiodo precursor **1**[20] with different arylethynyls, analogous to the reported procedure (Scheme 1).[19]

To our surprise, the synthesis of the 5,17-bisarylalkynylcalix[4]arenes **B1**–**B3** was initially complicated by the difficult accessibility of the diiodo precursor **2b**. Even though this compound has been mentioned in several synthetic procedures as the starting material, it has not to our knowledge actually been described and characterized properly. Some of the previous papers cite the diiodo starting material **2a** erratically as the bismethoxy derivative. Compound **2**[21] is iodinated in two repetitive steps by using excess benzyltrimethylammonium dichloroiodate (BTMA·ICl_2) in a dichloromethane/methanol mixture.[22] The extremely low solubility of **2a** hampered its purification and characterization significantly necessitating the complete characterization at the stage of the synthesis of tetrapropylated **2b**. The final cou-



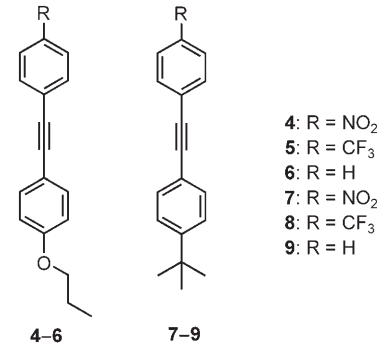
Scheme 1. Synthesis of the tetraalkynylcalix[4]arenes **A1**–**A3**.

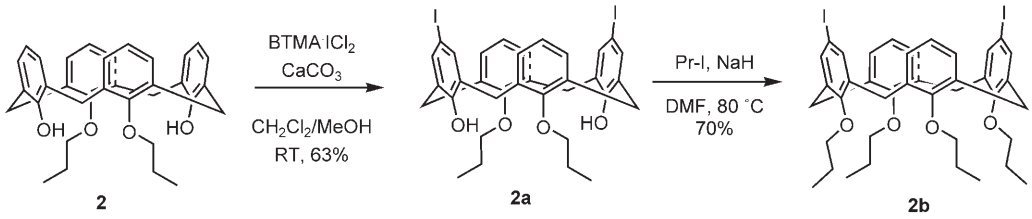
pling step proceeded smoothly to give compounds **B1**–**B3** in acceptable yields (Scheme 2). In the ^{13}C NMR spectrum, the methylene bridge carbons appear at $\delta = 30.9$ and 30.8 ppm for the type **A** and **B** calixarenes, respectively, which is indicative for the cone-conformation of these compounds in solution.

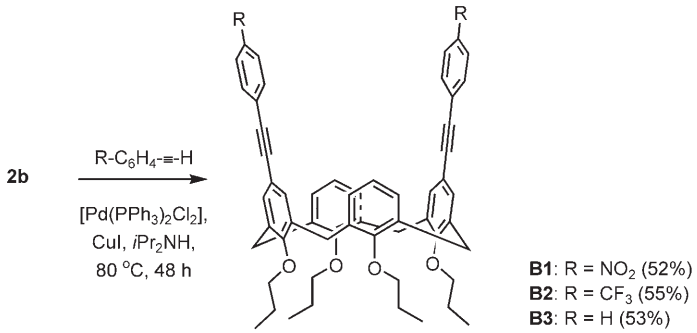
Type **C** calixarenes **C1**–**C3** were synthesized in the same manner as previously described.[23] The bistriflate **3**[24,25] was used as the starting compound and the Sonogashira reactions afforded the narrow-rim substituted intermediate compounds **3a**–**3c** in acceptable yields. To directly compare with the wide-rim substituted alkynyl-substituted calixarenes **B1**–**B3**, compounds **3a**–**3c** were converted into their corresponding *O*-propylated derivatives **C1**–**C3**, respectively (Scheme 3).

Linear spectroscopy: In accordance with the concept of treating the calixarenes as a covalent ensemble of dipolar subunits containing nonzero interdipolar angles and with no electronic communication between the subunits, the spectroscopic properties of the type **A**–**C** calixarenes were compared with the respective D–A-tolanes **4**–**9** which were prepared separately.

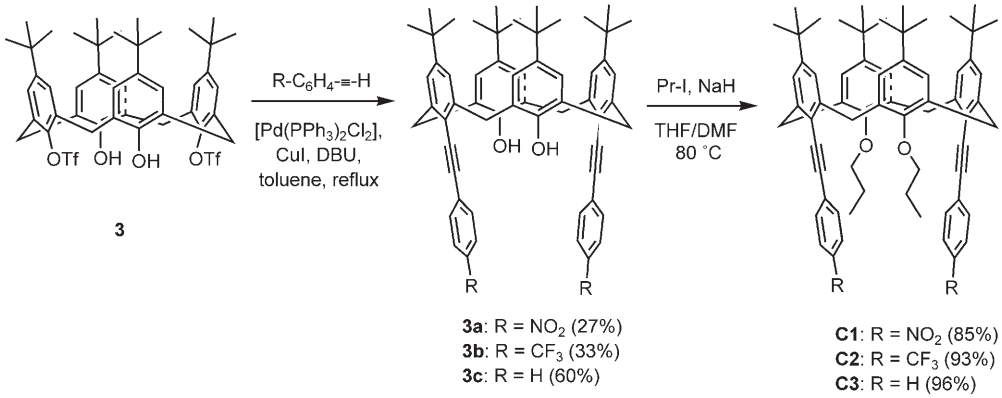
The absorption spectra of **A1**–**A3** and **B1**–**B3** confirmed this hypothesis. The spectral positions and the band characteristics can be interpreted as an additive composition of the







Scheme 2. Synthesis of the bisalkynylcalix[4]arenes **B1**–**B3**. Pr-I = 1-Iodopropane.



Scheme 3. Synthesis of the narrow-rimmed functionalized bisalkynylcalix[4]arenes **C1**–**C3**. DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene.

respective tolane absorptions. A broad, unstructured charge-transfer (CT) band, in particular, for each of the NO_2 derivatives (**A1**, **B1**, **C1**, **4**, **7**) reveals the pronounced CT character of these D–π–A systems. This behavior is observed to a lesser extent in the CF_3-substituted derivatives (**A2**, **B2**, **C2**, **5**, **8**) for which the absorption maxima are bathochromically shifted with respect to the phenylacetylenes (**A3**, **B3**, **C3**, **6**, **9**). As with the latter ones, they also display vibronic structuring of the low-energy absorption band (Figure 2). If one views these calixarenes as multichromophore assemblies, an important aspect to contemplate is the possibility of intramolecular dipole interactions, which can be conveniently assessed by UV/visible absorption spectroscopy.[26] The spectral shifts between the calixarenes and the corresponding tolane derivatives are small enough that the assumption of independent chromophores without electronic communication within the calixarene molecule can be considered valid. Nevertheless, in the type **C** subseries (**C1**–**C3**) it is notable that the differences between the absorption maxima of the calixarene **C1**–**C3** and the tolane reference compounds **7**–**9** increases with increasing acceptor strength of the terminal phenyl substituent from 6 (**C3** versus **9**) to 12 nm (**C2** versus **8**) and finally 19 nm (**C1** versus **7**). This result can be interpreted as an indication of some weak interaction between two adjacent subunits, especially when the individual solvation spheres are taken into consideration and the fact that the terminal phenylethynyl groups are kept in close proximity by the lower-rim substituted calixarene scaffold.[27]

Apart from these spectroscopic details, a more important observation is the scaling of the absorptive properties with the number of tolane subunits. With the difference in vibronic structure for the different compounds, the value for the extinction coefficient at the wavelength of maximal absorption might not be the best quantitative parameter to use, but the general trend is clearly observed, especially with the smooth spectra for the nitro compounds. When comparing the type **C** calixarene **C1** with the reference compound **7**, the ratio of the extinction coefficient is 2.0, while comparing the tetrasubstituted calixarene **C1** with the type **B** calixarene **B1**, this ratio is also 2.0. For the other compounds, the ratios may not be as perfect as expected, due to the effect of vibronic structure on the spectrum, but the same tendency is clearly observed, corroborating the assumption of electronic independent tolane subunits.

For the nitro-derivatives **A1**, **B1**, **C1**, **4**, and **7**, no fluorescence was observed either in the linear optical experiments (no one-photon excited emission spectra) or in the second-order nonlinear experiments for which no demodulation or phase shifts were observed in the HRS experiments). For the other compounds, weak emission was observed, with the concomitant red shift in the emission spectra for the CF_3-substituted **A2**, **B2**, **C2**, **5**, and **8** versus the unsubstituted **A3**, **B3**, **C3**, **6**, and **9**. Based on the absorption and fluorescence spectroscopic data, the transition dipole moments have been calculated. As can be seen in the Supporting Information, these results are in line with the experimental findings.

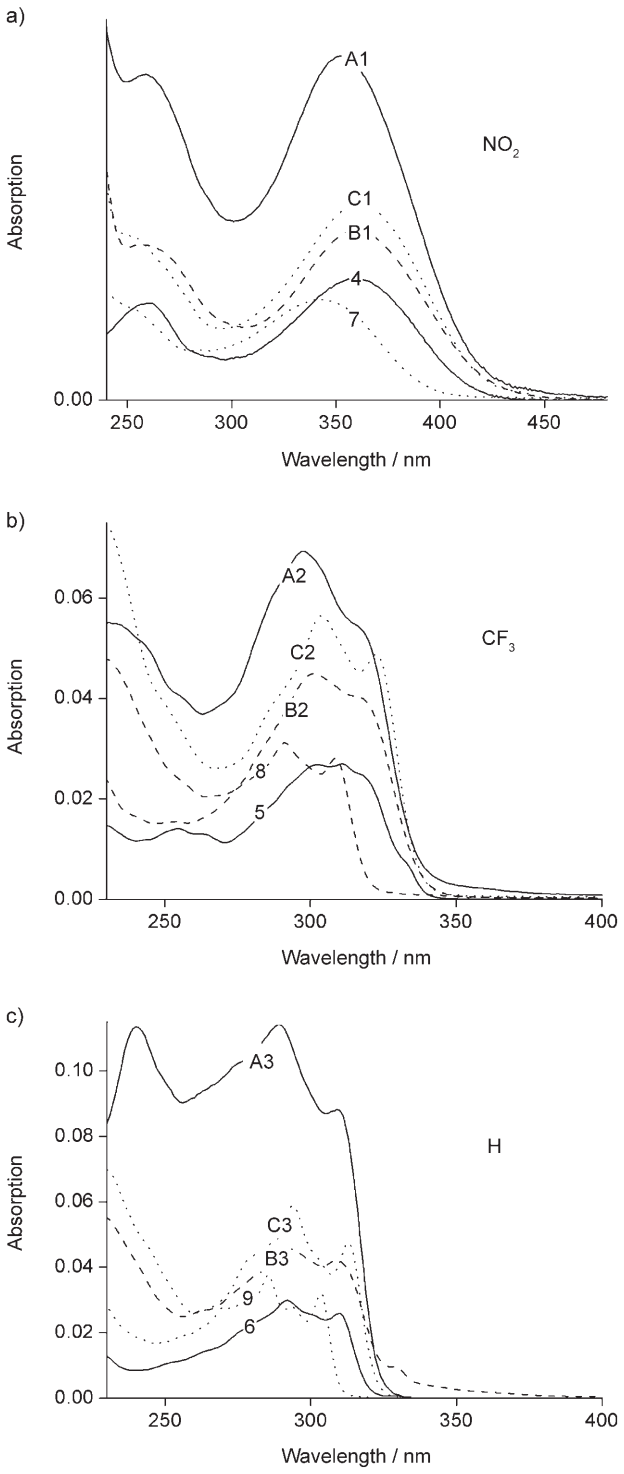


Figure 2. Absorption spectra of calixarenes **A1**–**A3**, **B1**–**B3**, **C1**–**C3**, and tolanes **4**–**9** measured in CH_2Cl_2, $c = 10^{-6}$ mol L^{-1}.

Second-order nonlinear optical properties: The second-order nonlinear polarizability, or first hyperpolarizability, β, of a single chromophore can be derived from the classic two-level formulation of β [Eq. (1)].[28]

$$\beta_n' = \frac{6(P_{ge})_n{}^2(\Delta\mu_{ge})_n(E_{op})_n{}^2}{[(E_{op})_n{}^2-(2E_{inc})^2][(E_{op})_n{}^2-E_{inc}{}^2]} \quad (1)$$

in which E_{op} is the energy of the optical (charge transfer) transition of interest and P_{ge} and $\Delta\mu_{ge}$ are the transition strength and ground-to-excited state dipole moment change associated with the charge-transfer absorption, respectively. A strong transition, with a large difference in dipole moment between ground and excited state, as encountered in charge-transfer chromophores, results in a substantial nonlinearity. The wavelength dependence is more intricate: A lower energy transition favors a larger β, yet the closeness of the transition wavelength to the measurement wavelength determines the degree of resonance enhancement. This two-level formalism also allows extracting the inherent static, wavelength-independent β_o from the dynamic, wavelength-dependent β.[29]

For the tolane reference compounds **4**–**9**, the β and β_o values can be rationalized in terms of the degree of charge transfer as a function of substituent (H, CF_3, or NO_2). The stronger the electron-withdrawing effect, increasing in the order $H < CF_3 < NO_2$, the lower the energy of the transition, the stronger the red-shift of the absorption, and the larger the value for β.[30] We also observed the effect of the lower electron-donor strength in the tolanes **7**–**9** with respect to the tolanes **4**–**6** in both the wavelength of the charge-transfer transition and the value of β. The depolarization ratio gives a good indication about the validity of the assumption that a single major hyperpolarizability tensor component dominates the NLO response. For dipolar CT molecules with the unique dipolar axis along the z dimension, β_{zzz} is dominant. When this is the case, the depolarization ratio ρ is larger than 2.5 and in the limiting case 5. This is clearly observed for the nonfluorescent compounds **A1**, **B1**, **C1**, **4**, and **7**, with a strikingly high value of 4.96 for the tetrasubstituted calixarene **A1**. Lower values for the depolarization ratio can point to off-diagonal tensor contributions in which there are additional hyperpolarizability tensor elements contributing to the NLO response or to another cause of the depolarization. The lowest value for ρ that can be achieved from off-diagonal contributions is 1.5 for purely octopolar molecular geometries. For the fluorescent tolane references, the even lower depolarization ratios (as low as 1.11) are clearly caused by fluorescence depolarization and do not convey information about hyperpolarizability tensor components.

Congruent with the analysis of the linear optical properties as originating from the appropriate number of noninteracting chromophores in the calixarenes, we can express the β_{zzz} in the calixarenes as resulting from the vector additions of the individual β_{mono} as $\beta_{zzz} = n(\cos\theta)^3\beta_{mono}$, with θ the opening angle between the chromophoric tolane subunits and $n=4$ for the tetra- and $n=2$ for the disubstituted calixarenes. This then results in a value for the opening angle θ. Please note that these values are essentially identical when using the static $\beta_{zzz,o}$ values, as the resonance enhancement factors within a series of model compound, di- and tetrasubstituted calixarenes, are very similar. The values for the opening angle θ for the di- and tetrasubstituted calixarenes as derived from HRS experiments are given in the last column of Table 1.

X-ray structure analysis: Single crystals suitable for X-ray structural determination were obtained for **A3** and **C3**, respectively (Figures 3 and 4). This allows a reliable comparison between the type **A** and **C** calixarenes in terms of the electronic situation of the tolane subunits, which have a similar D–A substitution.

For **A3**, the two opposite tolane subchromophores are held in an angle of 127 and 17°, respectively. Note that all four triple bonds permit both rotational and bending motions, such that none of the opposing acetylenic phenyl termini are in relative orientations indicative of attractive (π-stacking) interactions.

In the case of calixarene **C3**, the opening angle as subtended by the two opposite tolane subunits is approximately four degrees, while the planes of the two terminal phenyl

Table 1. Spectroscopic data for **A1**–**A3**, **B1**–**B3**, **C1**–**C3**, and **4**–**9** measured in CH_2Cl_2.

	λ_{max}(abs) [nm]	ε_{max} [cm^2mol^{-1}]	λ_{max}(em)[a] [nm]	φ[b]	τ [ns]	ρ	$\beta_{zzz,800}$ [10^{-30}esu]	$\beta_{zzz,0}$ [10^{-30}esu]	θ [°]
A1	353	76799	–	<0.01	–	4.96±0.09	530±20	94±4	43±2
A2	317	54870	382	0.03	1.1±0.2	1.36±0.08	100±20	31±25	23±7
A3	309	88221	368	0.01	3.0±0.1	1.11±0.01	80±10	27±3	33±6
B1	358	38250	–	<0.01	–	3.0±0.1	480±20	76±3	27±5
B2	315	40299	388	0.03	0.6±0.3	2.3±0.1	60±10	19±3	12±10
B3	309	42184	369	0.01	1.0±0.2	1.6±0.1	60±10	21±3	16±10
C1	362	43669	–	<0.01	–	2.91±0.05	670±130	96±19	16±10
C2	321	48745	363	0.18	1.5±0.5	1.8±0.1	46±6	14±2	0±10
C3	309	42814	343	0.36	0.7±0.1	2.4±0.1	59±4	20±1	0±10
4	357	27200	–	<0.01	–	4.02±0.09	340±40	55±6	–
5	318	24170	370	0.01	–	1.8±0.1	32±5	10±2	–
6	309	25819	349	<0.01	4±6	1.5±0.1	34±5	12±2	–
7	343	21543	–	<0.01	–	2.50±0.05	380±40	82±9	–
8	309	28102	337	0.02	1.8±0.3	2.3±0.1	22±2	7.6±0.7	–
9	303	31877	324	<0.01	1.8±0.3	1.5±0.1	28±3	10±1	–

[a] Excitation wavelength λ(ex) = 300 nm; the nitro compounds **A1**, **B1**, **C1**, **4**, and **9** are practically nonfluorescent. [b] Fluorescent quantum yields, Φ, were determined by using quinine sulphate in 0.1 N H_2SO_4 as standard.

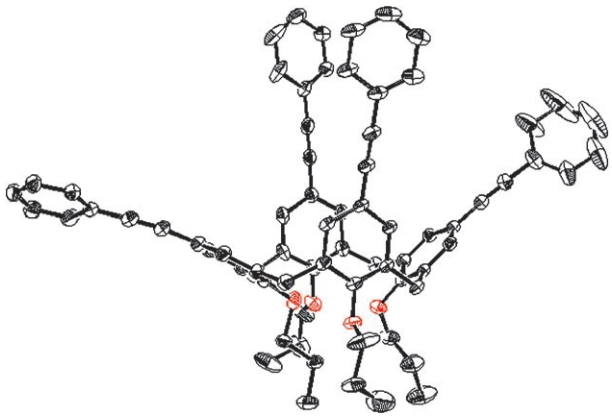


Figure 3. Structural diagram of calixarene **A1** (ORTEP, 50% probability ellipsoids). Hydrogen atoms have been omitted for clarity.

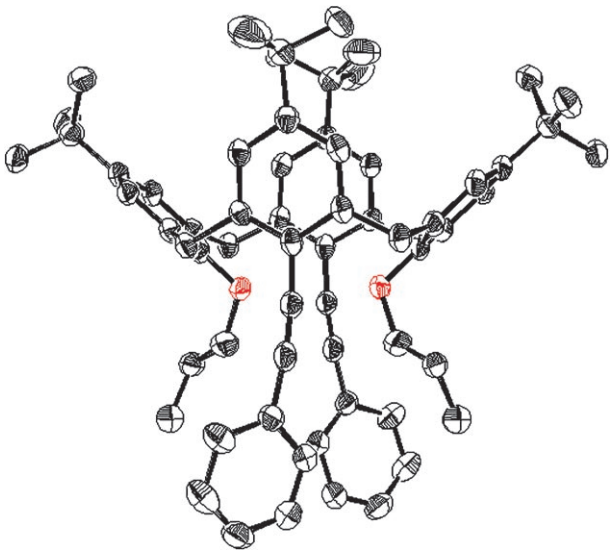


Figure 4. Structural diagram of calixarene **C1** (ORTEP, 50% probability ellipsoids). Hydrogen atoms have been omitted for clarity.

rings are not parallel to each other, but are titled inwards to each other by an angle of 18°. It is also evident that the triple bonds of the arylalkynyl moieties in **9** are bent with an average dihedral angle of 26°. The lower-rim *O*-propoxy groups contribute a considerable amount of steric bulk, supposedly obstructing a rapid "breathing" of the calixarene cavity.

Conclusion

A number of acetylene expanded calixarene-based deep-cavitands have been synthesized by Sonogashira-coupling, displaying elevated second-order nonlinearities. The important conclusion to be drawn from the spectroscopic investigations is that it is possible to derive a value for the opening angle θ from the hyperpolarizability values for the type **A**–**C** calixarenes, hence, HRS can be employed as an analytical tool for the structural determination of calixarenes in solution. Being aware of the limitations of treating the nonlinear optically-active calixarenes as an ensemble of isolated D–A chromophores,[31] this simplified model can be considered valid and useful for most of the (supramolecular) chemical issues addressed when working with calixarenes. Nevertheless, the consistently larger opening angles for the NO_2-substituted calixarenes observed point in this direction: The close proximity of strongly polar/polarizable subunits is avoided by larger opening angles. As a result of the steric conditions in each calixarene scaffold, consistently larger opening angles are found for the upper rim disubstituted type **B** calixarenes than for the lower rim, type **C**, disubstituted ones, while this angle is the largest for the tetrasubstituted, type **A** calixarenes. When comparing an average of a dynamic opening angle as obtained from HRS measurements in solution with the values observed in the solid state, good agreement is found for the lower-rim substituted **C3**. A very clear parallel arrangement of the two phenyl(ethynyl) moieties (opening angle 0°) is in good agreement with the findings in the X-ray structure. Despite the fact that for the type **A** calixarene **A1**, the discrepancy between the angles determined in solution and in the solid state is still within the error margin,[19] for compound **A3** the value of 33° in solution stands out against a value of 72° in the crystal. We attribute this difference to the crystal packing, for which the molecules of **A3** form columns of cone stacks. However, this case demonstrates once again the necessity of having a reliable analytical tool in hand to asses the structural features of the highly dynamic calixarene analytes in solution.

Experimental Section

General: All solvents and reagents were used as purchased. Ethynylaryls were purchased from Aldrich and used without further purification. TLC was performed on Alugram Sil G/UV 254-coated aluminum sheets (Macherey–Nagel) with UV detection at 254/365 nm. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer at 300 and 75 MHz, respectively, in deuterated chloroform (deuteration grade >99.80%) with the solvent signal serving as the internal standard. MS were recorded on a HP1100 MSD spectrometer. MALDI-TOF MS spectra were recorded on an Applied Biosystems DE-RP equipment. API-MS spectra were recorded with an Agilent 1100 series LC/MSD chromatographic system. Preparative thin-layer chromatography (PLC) was carried out using TLC high-purity silica as supplied by Aldrich with gypsum binder added. Elemental analyses were performed on a LECO CHNS 932 microanalyzer. Spectroscopic measurements were performed by using HPLC-quality solvents and are solvent corrected. UV/visible spectra were measured on a HP 8453 (Hewlett–Packard) spectrophotometer. A Perkin–Elmer LS50B luminescence spectrometer was employed for the fluorescence studies, in a four-sided quartz cell at RT in a right angle geometry and are corrected for the spectral response for the detection system.

Materials: The synthesis of **A1**, **A3**, **3c**, and **4** has been reported previously.[19,23]

5,17-Diiodo-bis-25,27-(*n*-propoxy)-26,28-dihydroxycalix[4]arene (2a): $CaCO_3$ (1.0 g) was added to a solution of **2** (509 mg, 1.0 mmol) and benzyltriammonium dichloroiodate (1.38 g, 4.0 mmol) in CH_2Cl_2/MeOH 5:3

(80 mL). After stirring at 25 °C for 24 h, the reaction was quenched by addition of HCl (conc, 2 mL). A solution of $NaHSO_3$ (10%, 20 mL) was added, the organic layer was separated, washed with water (3×20 mL), dried (Na_2SO_4), and then concentrated in vacuo. The resulting crude product was reacted again with benzyltriammonium dichloroiodate (1.38 g, 4.0 mmol) in the presence of $CaCO_3$ (1.0 mg) in CH_2Cl_2/MeOH 5:3 (80 mL) for 72 h at 25 °C. Following the workup described above, **2a** was produced as a crude product (479 mg) which was sufficiently pure to be employed in the next step. ^{1}H NMR: δ = 8.40 (s, 2H), 7.34 (s, 4H), 6.94–6.78 (m, 6H), 4.22 (d, J = 13.3 Hz, 4H), 3.95 (t, J = 7.8 Hz, 4H), 3.31 (d, J = 13.4 Hz, 4H), 2.08–2.01. (m, J = 8.0 Hz, 8H), 0.85 ppm (t, J = 7.5 Hz, 6H).

5,17-Diiodo-25,26,27,28-tetra-(*n*-propoxy)calix[4]arene (2b): NaH (200 mg, 5.0 mmol, 60% suspension in mineral oil) was added to a stirred solution of **2a** (380 mg, 0.5 mmol) in dry DMF (20 mL) and, after 45 min, *n*-propyliodide (488μL, 5.0 mmol) was also added. The reaction mixture was stirred at 80 °C for 24 h before it was quenched with HCl (1 M, 10 mL). The aqueous phase was extracted with CH_2Cl_2 and the separated organic layer was washed with 1 M HCl (10 mL), a sodium hydrogen sulphite solution (10%, 10 mL), water, and brine. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. The remaining solid was recrystallized from CH_2Cl_2/MeOH 10:1 to give pure **2b** as a colorless solid. Yield: 295 mg, 68%; R_f = 0.13 (hexanes); m.p. 204–209 °C; ^{1}H NMR: δ = 7.12 (s, 4H), 6.54–6.47 (m, 6H), 4.36 (d, J = 13.3 Hz, 4H), 3.86 (t, J = 7.8 Hz, 4H), 3.77 (t, J = 7.4 Hz, 4H), 3.09 (d, J = 13.4 Hz, 4H), 1.92–1.86 (m, 8H), 1.00 (t, J = 7.5 Hz, 6H), 1.00 ppm (t, J = 7.4 Hz, 6H); ^{13}C NMR: δ = 157.0, 155.9, 138.3, 137.1, 133.8, 128.2, 122.5, 85.5, 76.8, 76.3, 30.2, 23.3, 23.1, 10.4, 10.2 ppm; MALDI-TOF HRMS: m/z: calcd for $C_{40}H_{46}O_4Na$: 867.1386; found: 867.1378.

General procedure for the Sonogashira couplings yielding A1–A3, B1–B3, and 5–6: The respective iodoarene (0.25 or 0.5 mmol) was stirred together with $[Pd(PPh_3)_2Cl_2]$ (5 mol% per iodo group) and CuI (5 mol% per iodo group) in degassed diisopropylamine (10 mL) for 30 min at RT before the acetylene compound (1.5 mol equiv per iodo group) was added. The mixture was heated at 80 °C for the time specified. After this time, the solvent was removed and the remaining residue was suspended in water (50 mL) and extracted with EtOAc (3×20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude products were purified as described.

5,11,17,23-Tetrakis{[(4-trifluoromethyl)phenyl]ethynyl}-25,26,27,28-tetra(*n*-propoxy)calix[4]arene (A2): Reaction time: 48 h. The remaining solid was purified by column chromatography (hexanes/EtOAc 10:1) to give pure **A2** as pale-yellow plates. Yield: 189 mg, 60%; m.p. 163–165 °C. ^{1}H NMR: δ = 7.47 (d_{AB}, J = 8.6 Hz, 8H), 7.40 (d_{AB}, J = 8.6 Hz, 8H), 6.96 (s, 8H), 4.46 (d, J = 13.5 Hz, 4H), 3.90 (t, J = 7.5 Hz, 8H), 3.20 (d, J = 13.5 Hz, 4H), 1.94 (m, 8H), 1.01 ppm (t, J = 7.0 Hz, 12H); ^{13}C NMR: δ = 157.4, 155.5, 134.9, 132.0, 131.5, 127.3, 125.0, 116.3, 92.3, 87.0, 77.2, 30.8, 23.2, 10.3 ppm; MALDI-TOF MS: m/z: 1264 [M^+]; elemental analysis: calcd (%) for $C_{76}H_{60}O_4F_{12}$: C 72.15, H 4.78; found: C 71.67, H 4.91.

5,17-Bis[(4-nitrophenyl)ethynyl]-25,26,27,28-tetra(*n*-propoxy)calix[4]arene (B1): Column chromatography (hexanes/EtOAc 20:1) and final recrystallization from EtOH/toluene 1:1 gave pure **B1** as yellow crystals. Yield: 116 mg; 53%; R_f = 0.46 (hexanes/EtOAc 20:1); m.p. 245–247 °C; ^{1}H NMR: δ = 8.08 (d_{AB}, J = 8.1 Hz, 4H), 7.52 (d_{AB}, J = 8.1 Hz, 4H), 7.09 (s, 4H), 6.49 (brs, 6H), 4.46 (d, J = 13.4 Hz, 4H), 3.97 (t, J = 7.0 Hz, 4H), 3.80 (t, J = 7.0 Hz, 4H), 3.18 (d, J = 12.9 Hz, 4H), 1.93 (m, 8H), 1.08–0.97 ppm (m, 12H); ^{13}C NMR: δ = 158.7, 155.9, 146.5, 136.4, 133.7, 132.2, 131.9, 130.8, 128.1, 123.4, 122.3, 115.3, 95.9, 86.5, 76.9, 76.8, 30.9, 23.3, 23.2, 10.5, 10.1 ppm; MALDI-TOF HRMS: m/z: calcd for $C_{56}H_{54}O_8N_2$: 882.3875; found: 882.3839.

5,17-Bis{[(4-trifluoromethyl)phenyl]ethynyl}-25,26,27,28-tetra(*n*-propoxy)calix[4]arene (B2): Column chromatography (hexanes/EtOAc 20:1) and final recrystallization from EtOH gave pure **B2** as colorless crystals. Yield: 128 mg, 55%; m.p. 237 °C; ^{1}H NMR: δ = 7.54 (d_{AB}, J = 8.7 Hz, 4H), 7.50 (d_{AB}, J = 8.7 Hz, 4H), 7.13 (s, 4H), 6.49 (brs, 6H), 4.47 (d, J = 13.4 Hz, 4H), 3.99 (t, J = 7.7 Hz, 4H), 3.80 (t, J = 7.2 Hz, 4H), 3.20 (d, J = 13.4 Hz, 4H), 2.02–1.87 (m, 8H), 1.07 (t, J = 7.5 Hz, 6H), 0.98 ppm (t, J = 7.4 Hz, 6H); ^{13}C NMR: δ = 158.3, 155.8, 136.4, 133.6, 132.1, 131.5, 129.6, 129.2, 128.1, 125.1, 122.4, 115.7, 92.6, 86.7, 77.0, 76.9, 30.9, 23.4, 23.2, 10.5, 10.1 ppm; MALDI-TOF MS: m/z: 928 [M^+]; elemental analysis calcd (%) for $C_{58}H_{54}F_6O_4$: C 74.98, H 5.86; found: C 74.83, H 5.86.

5,17-Bis[(phenyl)ethynyl)]-25,26,27,28-tetra(*n*-propoxy)calix[4]arene (B3): Column chromatography (hexanes/EtOAc 20:1) and final recrystallization from EtOH gave pure **B3** as colorless crystals. Yield: 105 mg, 53%; m.p. 188–199 °C; ^{1}H NMR: δ = 7.54 (d_{AB}, J = 8.7 Hz, 4H), 7.50 (d_{AB}, J = 8.7 Hz, 4H), 7.13 (s, 4H), 6.49 (brs, 6H), 4.47 (d, J = 13.4 Hz, 4H), 3.99 (t, J = 7.7 Hz, 4H), 3.80 (t, J = 7.2 Hz, 4H), 3.20 (d, J = 13.4 Hz, 4H), 2.02–1.87 (m, 8H), 1.07 (t, J = 7.5 Hz, 6H), 0.98 ppm (t, J = 7.4 Hz, 6H); ^{13}C NMR: δ = 158.3, 155.8, 136.4, 133.6, 132.1, 131.5, 129.6, 129.2, 128.1, 125.1, 122.4, 115.7, 92.6, 86.7, 77.0, 76.9, 30.9, 23.4, 23.2, 10.5, 10.1 ppm; MALDI-TOF MS: m/z: 792 [M^+]; elemental analysis: calcd (%) for $C_{56}H_{54}O_4 \cdot 1/2\,H_2O$: C 83.86, H 7.16; found: C 83.82, H 7.14.

5,11,17,23-Tetra(*tert*-butyl)-26,28-bis(*p*-nitrophenylethynyl)calix[4]arene (3a): A solution of DBU (66.9 mg, 0.44 mmol) and 1-ethynyl-4-nitrobenzene (35.3 mg, 0.24 mmol) in dry toluene (3 mL) were added to a stirred mixture of (*p-tert*-butylcalix[4]arene-1,3-bistriflate) (100.0 mg, 0.11 mmol), $[PdCl_2(PPh_3)_2]$ (5.0 mg, 0.007 mmol), and CuI (1.0 mg, 0.005 mmol) in dry toluene (10 mL) at reflux temperature. The resulting mixture was stirred for 24 h at the reflux temperature, cooled, and then poured into saturated aqueous ammonium chloride (20 mL) and washed with H_2O (20 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by PLC (EtOAc/hexanes 1:99) to give **3a** (53 mg, 27%); m.p. 145–147 °C; ^{1}H NMR: δ = 7.89 (d_{AB}, J = 8.0 Hz, 4H), 7.54 (d_{AB}, J = 8.0 Hz, 4H), 7.18 (s, 4H), 6.79 (s, 4H), 5.29 (s, 2H), 4.56 (d, J = 14.0 Hz, 4H), 3.65 (d, J = 14.0 Hz, 4H), 1.33 (s, 18H), 0.91 ppm (s, 18H); ^{13}C NMR: δ = 152.4, 152.2, 151.3, 147.0, 143.1, 142.1, 132.0, 130.2, 128.5, 125.8, 124.7, 123.6, 117.8, 95.6, 93.2, 37.1, 34.6, 34.2, 31.9, 30.8 ppm; MS (APCI+): m/z: calcd for $C_{60}H_{62}N_2O_6$: 907.16 [M^+]; found: 907.50.

5,11,17,23-Tetra(*tert*-butyl)-25,27-dipropoxy-26,28-bis(*p*-nitrophenylethynyl)calix[4]arene (C1): NaH (6.4 mg, 0.265 mmol) was added to a solution of **3a** (60 mg, 0.066 mmol) in anhydrous DMF (1 mL) and THF (10 mL), followed by the addition of *n*-propyliodide (45.1 mg, 0.265 mmol). The resulting mixture was heated at reflux temperature for 6 h. After this time, the mixture was cooled to RT and the THF was evaporated in vacuo. The residue was then added to H_2O (10 mL) to give a yellow precipitate which was purified by PLC (60% CH_2Cl_2 in petroleum ether) to give **C1**. Yield: 55.6 mg, 85%; m.p. >330 °C; ^{1}H NMR: δ = 8.20 (d_{AB}, J = 8.0 Hz, 4H), 7.61 (d_{AB}, J = 8.0 Hz, 4H), 7.27 (s, 4H), 6.56 (s, 4H), 4.68 (d, J = 12.5 Hz, 4H), 4.08–4.05 (m, 4H), 3.49 (d, J = 12.5 Hz, 4H), 2.13–1.86 (m, 4H), 1.39 (s, 18H), 0.86 (s, 18H), 0.51–0.48 ppm (m, 6H); ^{13}C NMR: δ = 154.0, 150.8, 146.6, 146.0, 142.6, 135.6, 132.0, 131.6, 126.3, 123.9, 123.7, 118.3, 97.8, 97.5, 92.3, 75.5, 36.6, 34.4, 32.0, 31.0, 23.0, 9.9 ppm; MS (APCI+): m/z: calcd for $C_{66}H_{74}N_2O_6$: 991.3 [M^+]; found: 991.5.

5,11,17,23-Tetra(*tert*-butyl)-26,28-bis[*p*-(trifluoromethyl)phenylethynyl]-calix[4]arene (3b): A solution of DBU (66.9 mg, 0.44 mmol) and 4-ethynyl-α,α,α-trifluorotoluene (40.8 mg, 0.24 mmol) in dry toluene (3 mL) were added to a stirred mixture of *p-tert*-butylcalix[4]arene-1,3-bistriflate (100 mg, 0.11 mmol), $[PdCl_2(PPh_3)_2]$ (5.0 mg, 0.007 mmol), and CuI (1 mg, 0.005 mmol) in dry toluene (10 mL) at reflux temperature. The resulting mixture was stirred for 24 h at the reflux temperature, cooled, and then poured into saturated aqueous ammonium chloride (20 mL) and washed with H_2O (20 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by PLC (CH_2Cl_2/petroleum ether 3:7) to give **3b**. Yield: 24.1 mg, 23%; m.p. 271–273 °C; ^{1}H NMR: δ = 7.53 (d_{AB}, J = 8.5 Hz, 4H), 7.33 (d_{AB}, J = 8.5 Hz, 4H), 7.16 (s, 4H), 6.78 (s, 4H), 5.33 (s, 2H), 4.58 (d, J = 14.0 Hz, 4H), 3.63 (d, J = 14.0 Hz, 4H), 1.31 (s, 18H), 0.91 ppm (s, 18H); ^{13}C NMR: δ = 151.7, 151.2, 142.8, 142.0, 131.8, 130.4, 128.5, 127.2, 125.8, 125.4, 124.6, 122.9, 118.3, 95.9, 89.9, 37.1, 34.5, 34.2, 31.9, 30.9 ppm; MS (APCI+): m/z: calcd (%) for $C_{62}H_{62}F_6O_2$: 953.16 [M^+]; found: 953.50.

5,11,17,23-Tetra(*tert*-butyl)-25,27-dipropoxy-26,28-bis(*p*-trifluoromethylphenylethynyl)calix[4]arene (C2): NaH (4.8 mg, 0.20 mmol) was added to a solution of **3b** (50 mg, 0.05 mmol) in anhydrous DMF (1 mL) and THF (10 mL), followed by the addition of *n*-propyliodide (34.0 mg,

0.20 mmol). The reaction was then conducted as with **7**, giving a pale-white precipitate, which was purified by PLC (CH_2Cl_2/petroleum ether 1:3) to give **C2**. Yield: 48.2 mg, 93%; m.p. >300°C; ^{1}H NMR: δ=7.58–7.57 (m, 8H), 7.19 (s, 4H), 6.54 (s, 4H), 4.71 (d, J=12.5 Hz, 4H), 4.10–4.07 (m, 4H), 3.45 (d, J=12.5 Hz, 4H), 2.01–1.93 (m, 4H), 1.37 (s, 18H), 0.85 (s, 18H), 0.48–0.44 ppm (m, 6H); ^{13}C NMR: δ=154.1, 150.1, 145.8, 142.3, 135.9, 131.4, 126.2, 125.4, 123.6, 123.1, 118.7, 99.8, 94.3, 92.1, 76.5, 36.7, 34.4, 34.3, 32.0, 31.0, 22.8, 9.7 ppm (one missing carbon resonance in the aromatic region); MS (APCI+): m/z: calcd for $C_{60}H_{62}N_2O_6$: 1037.3 [M^+]; found: 1037.7.

5,11,17,23-Tetra(*tert*-butyl)-25,27-dipropoxy-26,28-bis(phenylethynyl)calix[4]arene (C3): NaH (5.8 mg, 0.24 mmol) was added to a solution of **3c** (50 mg, 0.06 mmol) in anhydrous DMF (1 mL) and THF (10 mL), followed by the addition of *n*-propyliodide (40.8 mg, 0.24 mmol). The reaction was then conducted as for **7**, giving a pale-yellow precipitate, which was purified by PLC (hexanes/EtOAc 10:1) to give **C3**. Yield: 51.9 mg, 96%; m.p. >300°C; ^{1}H NMR: δ=7.53 (d_{AB}, J=7.5 Hz, 4H), 7.32–7.28 (m, 6H), 7.18 (s, 4H), 6.53 (s, 4H), 4.77 (d, J=12.5 Hz, 4H), 4.16–4.13 (m, 4H), 3.44 (d, J=12.5 Hz, 4H), 2.02–1.97 (m, 4H), 1.38 (s, 18H), 0.86 (s, 18H), 0.47–0.44 ppm (m, 6H); ^{13}C NMR: δ=154.2, 149.3, 145.6, 142.1, 136.3, 131.4, 128.2, 127.5, 126.0, 125.2, 123.4, 119.5, 93.3, 91.5, 76.5, 36.7, 34.4, 34.2, 32.0, 31.0, 22.7, 9.6 ppm; MS (APCI+): m/z: calcd for $C_{66}H_{76}O_2$: 901.3 [M^+]; found: 901.5.

4-[(4-Propoxyphenyl)ethynyl]trifluoromethylbenzene (5): Column chromatography (hexanes/EtOAc 20:1) and final recrystallization from EtOH gave pure **5** as yellow needles. Yield: 117 mg, 77%; m.p. 105°C; ^{1}H NMR: δ=7.63–7.59 (m, 4H), 7.48 (d_{AB}, J=8.9 Hz, 2H), 6.89 (d_{AB}, J=8.9 Hz, 2H), 3.94 (t, J=6.5 Hz, 2H), 1.84 (m, 2H), 1.05 ppm (t, J=7.4 Hz, 3H); ^{13}C NMR: δ=159.7, 133.2, 132.8, 131.6, 125.5, 125.3, 125.2, 114.6, 114.3, 92.1, 86.8, 69.6, 22.5, 10.5 ppm; HRMS (EI+): m/z: calcd for $C_{18}H_{15}OF_3$: 304.1075; found: 304.1079.

[(4-Propoxyphenyl)ethynyl]benzene (6): Column chromatography (hexanes/EtOAc 20:1) and final recrystallization from EtOH gave pure **6** as pale-yellow plates. Yield: 96 mg, 81%; m.p. 64°C; ^{1}H NMR: δ=7.63–7.59 (m, 4H), 7.48 (d_{AB}, J=8.4 Hz, 2H), 6.89 (d_{AB}, J=8.4 Hz, 2H), 3.94 (t, J=6.6 Hz, 2H), 1.84 (sex., J=7.2 Hz, 2H), 1.07 ppm (t, J=7.4 Hz, 3H); ^{13}C NMR: δ=159.2, 133.0, 131.4, 128.3, 127.8, 123.6, 115.1, 114.5, 89.5, 87.9, 69.5, 22.5, 10.5 ppm; MS (EI+): m/z: 236 (53) [M^+]; elemental analysis: calcd (%) for $C_{17}H_{16}O$: C 86.40, H 6.82; found: C 85.89, H 6.75.

4-[(4-*tert*-Butylphenyl)ethynyl]nitrobenzene (7): A mixture of 1-bromo-4-*tert*-butylbenzene (106.5 mg, 0.5 mmol), 1-ethynyl-4-nitrobenzene (87.2 mg, 0.60 mmol), and [$PdCl_2(PPh_3)_2$] (17.6 mg, 0.025 mmol) in dry degassed triethylamine (5 mL) was stirred at RT for 20 min, after which time, CuI (3.8 mg, 0.02 mmol) was added. The resulting mixture was stirred at reflux for 1 h and, after cooling, the solvent was evaporated in vacuo. The residue was then dissolved in EtOAc (10 mL) and washed with H_2O (15 mL). The organic layer was dried ($MgSO_4$), filtered, and the residue was purified by PLC (CH_2Cl_2/petroleum ether 1:1) to give **7**. Yield: 83.0 mg, 60%; m.p. 145–146°C; ^{1}H NMR: δ=8.22 (d_{AB}, J=8.5 Hz, 2H), 7.66 (d_{AB}, J=8.5 Hz, 2H), 7.50 (d_{AB}, J=8.0 Hz, 2H), 7.41 (d_{AB}, J=8.0 Hz, 2H), 1.35 ppm (s, 9H); ^{13}C NMR: δ=153.0, 147.2, 132.4, 131.9, 130.9, 125.8, 123.9, 119.3, 95.3, 87.3, 35.2, 31.4 ppm; GCMS: m/z: calcd for $C_{18}H_{17}NO_2$: 279.3 [M^+]; found: 279.0.

4-[(4-*tert*-Butylphenyl)ethynyl]trifluoromethylbenzene (8): Tetrabutylammonium fluoride (392.2 mg, 1.50 mmol) and H_2O (27.5 mg, 1.50 mmol) were added to a stirred mixture of 1-bromo-4-*tert*-butylbenzene (106.5 mg, 0.5 mmol), 4-ethynyl-α,α,α-trifluorotoluene (102.1 mg, 0.60 mmol), and [$PdCl_2(PPh_3)_2$] (10.5 mg, 0.015 mmol) under argon at RT. The resulting mixture was stirred for 3 h at 80°C, then cooled, dissolved in H_2O (10 mL), and extracted with EtOAc (2×10 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by PLC (hexanes/EtOAc 20:1) to give **8**. Yield: 59.0 mg, 39%; m.p. 121–123°C; ^{1}H NMR: δ=7.62 (d_{AB}, J=8.5 Hz, 2H), 7.59 (d_{AB}, J=8.5 Hz, 2H), 7.48 (d_{AB}, J=8.5 Hz, 2H), 7.39 (d_{AB}, J=8.5 Hz, 2H), 1.33 ppm (s, 9H); ^{13}C NMR: δ=152.6, 132.0, 131.7, 130.1, 127.6, 125.7, 125.5, 123.1, 119.8, 92.2, 87.6, 35.1, 31.4 ppm; GCMS: m/z: calcd for $C_{19}H_{17}F_3$: 302.33 [M^+]; found: 302.0.

4-[(4-*tert*-Butylphenyl)ethynyl]benzene (9): Tetrabutylammonium fluoride (784.4 mg, 3.00 mmol) and H_2O (54 mg, 3.00 mmol) were added to a stirred mixture of 1-bromo-4-*tert*-butylbenzene (213.0 mg, 1.00 mmol), phenylacetylene (122.4 mg, 1.20 mmol), and [$PdCl_2(PPh_3)_2$] (21.0 mg, 0.03 mmol) under argon at RT. The resulting mixture was stirred for 1.5 h at 80°C and was then cooled. H_2O (10 mL) was added and then extracted with Et_2O (2×10 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by PLC (hexanes/EtOAc 20:1) to give **9**. Yield: 70.0 mg, 30%; m.p. 62–63°C; ^{1}H NMR: δ=7.53–7.46 (m, 5H), 7.38–7.31 (m, 4H), 1.33 ppm (s, 9H); ^{13}C NMR: δ=151.8, 131.8, 131.6, 128.5, 128.3, 125.6, 123.8, 120.5, 89.8, 88.9, 35.0, 31.4 ppm; GCMS: m/z: calcd for $C_{18}H_{18}$: 234.1 [M^+]; found: 234.2.

X-ray crystallographic analysis

*Summary for **A1***: Colorless prisms were obtained from toluene; space group=$P2_1/n$; Z=4 in a cell of dimensions: a=13.5384(16), b=33.194(4), c=14.7531(18) Å; α=90.00, β=116.842(3), γ=90.00°; V=5915.6(12) Å^3; ρ_{calcd}=1.138 g cm^{-3}; μ=0.069 mm^{-1}; F(000)=2152. A total of 28568 reflections were measured, 17877 unique, by using graphite monochromatized $Mo_{K\alpha}$ radiation (λ=0.71073 Å) at 100 K. The structure was refined on F^2 to R_w=0.1520 with a goodness-of-fit=1.018 for 764 refined.

*Summary for **C1***: Colorless platelet crystals were obtained from $CHCl_3$/MeOH; monoclinic; space group=$P2_1/n$; Z=4 in a cell of dimensions: a=13.002(3), b=24.016(5), c=17.003(4) Å; α=90.00, β 118.442(6), γ=90.00°; V=5441(2) Å^3; ρ_{calcd}=1.225 g cm^{-3}; μ=0.064 mm^{-1}; F(000)=1952. A total of 4821 reflections were measured, 4402 unique, by using graphite monochromatized $Mo_{K\alpha}$ radiation (λ=0.71073 Å) at 113 K. The structure was refined on F^2 to R_w=0.3323 with a goodness-of-fit=1.117 for 596 refined parameters.

CCDC-641917 and -643528 contain the supplementary crystallographic data for these compounds, respectively. These data can be obtained free of charge from The Cambridge Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Second-order nonlinear optical (HRS) measurements: The second-order nonlinear optical polarizability, or first hyperpolarizability of potentially fluorescent chromophores has to be measured by frequency-resolved femtosecond HRS.[32] If no attention is devoted to the potential multiphoton fluorescence contribution to the HRS signal, a systematic overestimation of β can result.[33] This systematic error can be avoided by making the distinction between immediate scattering and time-delayed fluorescence in the spectral domain (spectrally broad fluorescence versus sharp scattering at the second-harmonic of the laser line only), in the time domain (a nanosecond fluorescence tail following the femtosecond laser pulse excitation),[34] or in the frequency domain. In the latter approach, the fluorescence is demodulated (diminished in amplitude) and acquires a phase shift with respect to scattering only. We have implemented this frequency-domain technique and determined the high-frequency limit of the HRS signal. This signal was then free of fluorescence and was used to retrieve an accurate, fluorescence-free β value.[35] As the reference compound to determine hyperpolarizability values at 800 nm, crystal violet in methanol was used ($\beta_{xxx,800}=338\times10^{-30}$ esu). In the analysis, the difference between the octopolar symmetry of crystal violet and the dipolar symmetry of the compounds **A1**–**A3**, **B1**–**B3**, **C1**–**C3**, and **4**–**9**, as well as the different solvents were taken into account. An additional experimental parameter that can be determined by HRS is the nonlinear depolarization ratio, that is, the ratio between the HRS intensity for parallel (vertical) and perpendicular (horizontal) polarization in the detection (vertical polarization for the excitation).[36] This ratio is 5 in the limit of a single major (dipolar) hyperpolarizability tensor component (diagonal β_{zzz} tensor element along the dipolar molecular z axis) and infinitely small numerical aperture. This ratio can be as low as 1.5 for purely octopolar structures and in the case the off-diagonal component β_{zxx} is just as large as the diagonal β_{zzz}. Multiphoton fluorescence has a much more pronounced effect on the value of the depolarization ratio. As the emission is occurring nanoseconds after the excitation, the fluorescence contribution to the HRS signal can be strongly depolarized, resulting in a ratio as low as 1.[37]

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