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A Triphenylene Scaffold with C_{3V}-symmetry and Nanoscale Dimensions

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Abstract: The synthesis and characterization of a new scaffold for molecular recognition and combinatorial chemistry is presented. Oxidative trimerization of certain catechol ketals with $MoCl_5$ gives a statistical mixture of isomers. The applicability of these molecules for combinatorial chemistry is shown and initial steps toward a new class of synthetic receptors are reported. © 1999 Elsevier Science Ltd. All rights reserved.

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Structures with a rigid skeleton and directed functional groups are useful tools in molecular recognition. We have a long-standing interest in C_3 and C_{3V} symmetric[1] scaffolds with three functional groups (FG, Figure 1) that appear on the same face of the molecule.[2] Such structures have been used in combinatorial chemistry,[3] synthetic receptors,[4] and peptide bundles.[5] The size and rigidity of the triphenylene skeleton offers some advantages over existing systems. For example, in Figure 1, the ca. 10 Å distance between the side-chains is almost twice that of other tripodal platforms[6] and is greater than those in resorcinarenes[7] or tetraaryl porphyrins,[8] structures much-admired in supramolecular chemistry.

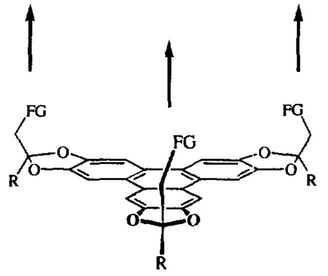

Figure 1. General structure of an all-*syn* functionalized triphenylene ketal.

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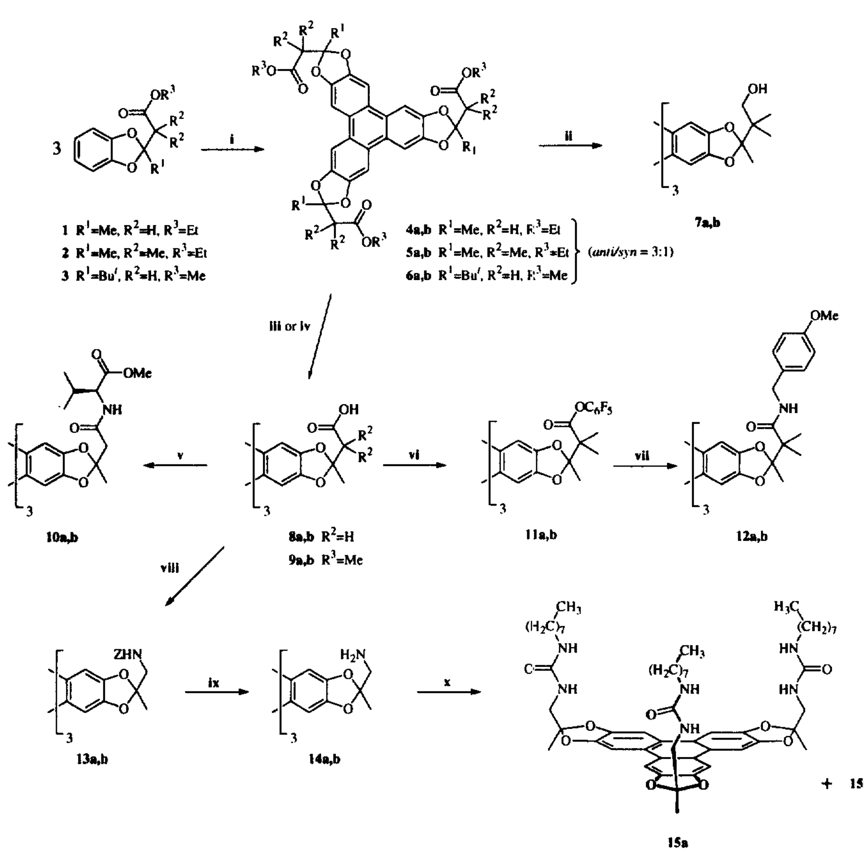
Hexaalkoxytriphenylenes are used as discotic mesogens[9] or optoelectronic devices,[10] but their syntheses are limited to structures with substitutents oriented **in** the aromatic plane.[11]

Conventional triphenylene syntheses are performed by oxidative trimerization in strongly acidic media such as $FeCl_3$/70% sulfuric acid[12] or choranil/70% sulfuric acid.[13] Because ketals do not tolerate these conditions, we first tried the ketalization of 2,3,6,7,10,11-hexahydroxytriphenylene. There is only one literature example which uses acetone in the presence of P_4O_{10}.[14] but these conditions were unsuccessful for other ketones. Only traces of ketalized triphenylene were found by using ethyl 3,3-dichloro-3-phenylpyruvate with hexahydroxytriphenylene under basic conditions.[15]



Scheme 1. Syntheses of triphenylene ketal derivatives. Reaction conditions and yields: **i.** $MoCl_5$, CH_2Cl_2, 21% for **4a,b**, 40% for **5a,b**, 32% for **6a,b**; **ii.** $LiAlH_4$, Et_2O, 93%; **iii.** LiOH, THF-H_2O, 81%; **iv.** Bu^tOK, H_2O-Et_2O, 72h, 93%; **v.** H-Val-OMe, BOP, Pr^i_2NEt, THF, 75%; **vi.** C_6F_5OH, EDC, 98%; **vii.** *p*-methoxy-benzylamine, CH_2Cl_2, 99%; **viii.** DPPA, NEt_3, BnOH, 48%; **ix.** cyclohexa-1,4-diene, Pd/C 10%, 98%; **x.** octylisocyanate, CH_2Cl_2, 39%.

Kumar *et al.* recently reported the oxidative trimerization of catechol ethers with $MoCl_5$ in CH_2Cl_2.[16] Although $MoCl_5$ is known to cleave ketals, the trimerization was successful on the ketals **1–3**. These catechols were synthesized by ketalization of catechol with the corresponding *β*-oxo ester in the presence of *p*-

toluenesulfonic acid using a Dean-Stark trap.[15] On multigram scales the trimerization yields varied between 20 and 40 %. The triphenylene ketals **4-6** were isolated as the main products[17] if the reaction is terminated after 20 min; shorter reaction times lead to the recovery of considerable starting material.

In all cases a statistical 3:1 mixture of *anti,anti,syn* to all-*syn* products were obtained. The isomeric mixtures **4a,b** and **5a,b** were separated by HPLC. In addition to similar chromatographic properties, **4a** and **4b** show identical ^{1}H-NMR (600 MHz) and ^{13}C-NMR (151 MHz) spectra in $CDCl_3$. The *t*-butyl groups in the R^1-position of **6a,b** allowed separation of the isomers by silica-gel chromatography. The all-*syn* isomer **4b** could be obtained by fractional crystallization from CH_2Cl_2/hexane. Its stereochemistry was verified by an X-ray crystal structure analysis.[18] The ORTEP plot of **4b** (Figure 2a) shows the three ester groups turned inwards and features a slight distortion of the aromatics from coplanarity.[19] The unit cell contains two molecules of **4b**, π-π stacked face-to-face in a staggered geometry (Figure 2b).[20] The ester groups of the molecules interdigitate with one another, resulting in an (up-down)$_3$ pattern.

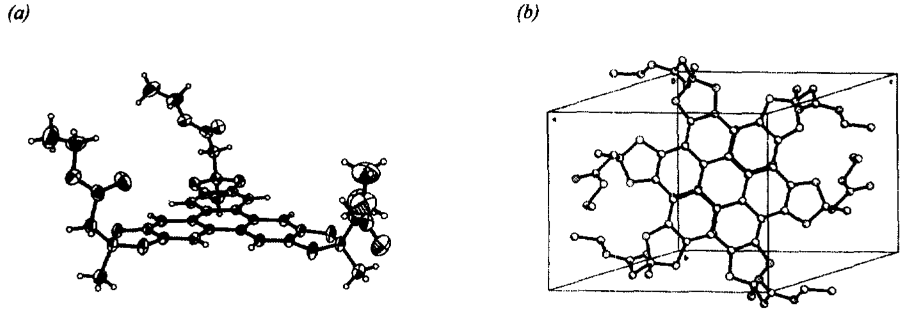


Figure 2. *(a)* ORTEP plot of **4b**. Non-hydrogen atoms are drawn with 30% probability ellipsoids. Hydrogen atoms are included in their ideal positions. *(b)* Unit cell packing diagram of **4b**. Hydrogen atoms are omitted for clarity.

Several derivatives of this new class of compounds were synthesized (Scheme 1). The isomeric mixture **5a,b** was saponified (KO^{t}Bu, H_2O, ether)[21] in 93% yield, the drastic conditions being required by the steric hindrance of the ester group. Coupling of *p*-methoxy-benzylamine via the penta-fluorophenylester gave **12a,b** in 97% overall yield. Using a mixture of different amines and the all-*syn* functionalized pentafluorophenylester **11b**, it is possible to produce libraries cleanly. Saponification of the mixture **4a,b** was possible with LiOH in 81% yield, and valine was coupled to the acids **8a,b** using BOP as the coupling reagent.

The triphenylene esters **4-6** all show interactions with electron poor π-systems like quinones and nitrated aromatics, characterized by a charge-transfer band in the visible region.[22] This interaction makes these structures candidates for synthetic receptors. For functional group elaboration, the protected triamine **14a,b** was prepared from **8a,b** using a Curtius rearrangement.[23] Subsequent reaction with octylisocyanate gave the trisurea mixture **15a,b** which could be separated by HPLC.

In conclusion we have shown that all-*syn* functionalized triphenylene ketals are accessible from their catechol ketals. Further investigations will be reported in due course.

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17. Detailed experimental procedures and full analytical data will be given in a later paper. Selected analytical data: **4a** and also **4b**: ^{1}H-NMR (600 MHz, $CDCl_3$): δ (ppm) = 7.72 (s, 6H), 4.16 (q, 6H, $^3J = 7.1$ Hz), 3.07 (s, 6H), 1.93 (s, 9H), 1.20 (t, 9H, $^3J = 7.1$ Hz); ^{13}C-NMR (151 MHz, $CDCl_3$): δ (ppm) = 167.95, 147.25, 124.48, 116.83, 101.74, 60.32, 43.38, 24.81, 13.78; HRMS (FAB, M + H$^+$): calcd. for $C_{36}H_{37}O_{12}^+$: 660.2207, found: 660.2229. **5a** (*anti,anti,syn*): ^{1}H-NMR (600 MHz, $CDCl_3$): 7.71 (s, 2H), 7.70 (s, 4H), 4.10-4.20 (m, 6H), 1.80 (s, 6H), 1.79 (s, 3H), 1.42 (s, 12H), 1.42 (s, 6H), 1.18-1.23 (m, 9H). **5b** (all-*syn*): ^{1}H-NMR (600 MHz, $CDCl_3$): 7.71 (s, 6H), 4.15 (q, $^3J = 7.1$ Hz, 6H), 1.80 (s, 9H), 1.41 (s, 18H), 1.22 (t, $^3J = 7.0$ Hz, 9H).
18. *Crystal data* for **4b**: $C_{36}H_{36}O_{12}$, $M = 660.65$, colorless parallelepipeds, 0.22 × 0.19 × 0.14 mm, triclinic, space group $P\bar{1}$, $a = 11.974(2)$, $b = 12.730(2)$, $c = 13.221(3)$ Å, $\alpha = 106.70(2)°$, $\beta = 98.89(2)°$, $\gamma = 113.62(2)°$, $U = 1682.9(6)$ Å^3, $Z = 2$, $D_c = 1.304$ g cm^{-1}, $\mu = 0.821$ mm^{-1}, $F(000) = 696$. The 5274 total reflections were collected at 296 K and at a wavelength of $\lambda = 1.54178$ Å and converged at $R_1 = 0.0759$, $wR_2 = 0.2325$.
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