

Spherands with Functional Groups in the Outer Sphere: Synthesis from Modified 1,1':3',1''-Terphenyls

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Two spherands (**1a,c**), functionalized in the outer sphere, have been synthesized by oxidative coupling of the dianions of terphenyls; these terphenyls are obtained by aldol condensation of 1,3-diarylpropanones with nitromalonaldehyde.

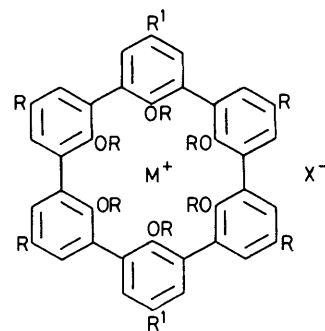
Recently Cram *et al.*¹ have developed a new type of highly structured cation complexing molecule that has an enforced cavity, the so-called spherand (**1**). These compounds form strong complexes with Li⁺ and Na⁺ ions with free energies of complexation of ≥ 23 and 19 kcal mol⁻¹,[†] respectively.² Our interest in the strong and selective complexation of these cations and the possible application of such complexes in biological systems as lipophilic cation carriers prompted us to synthesize spherands of this type that bear functional reactive groups in the outer sphere of the molecule. For this purpose we have developed a new synthetic route to substituted 1,1':3',1''-terphenyls which can be converted into the corresponding spherands by oxidative coupling of two such molecules. This has limitations because of the functional groups present which have to be stable in the presence of strong bases (BuⁿLi or Bu^sLi) and the radicals formed from the oxidation of the arylanions.

p-Methylanisole was acylated³ to give (**2a**), which was converted *via* a Willgerodt-Kindler rearrangement⁴ into (**2b**) with an overall yield of 52%. Selective bromination of (**2b**) with *N*-bromosuccinimide in dimethylformamide gave (**3a**)[‡] (88%, m.p. 132–133 °C) which was esterified to yield (**3b**)[‡] (EtOH, H⁺, 88%, b.p. 110–112 °C, 0.05 mmHg). Alkylation of the phenol with MeI and base gave (**3c**)[‡] (95%, b.p. 99–101 °C, 0.04 mmHg). Claisen condensation with isopropylmagnesium bromide as base afforded the β -keto-ester (**4a**) which was decarboxylated without further purification to yield (**4b**)[‡] (76%, m.p. 65–66 °C). The 1,1':3',1''-terphenyl (**5a**)[‡] was obtained by the reaction of (**4b**) with nitromalonaldehyde sodium salt in water-ethanol at 45 °C⁵ (75%, m.p. 168–169 °C). Oxidation of the nitrophenol (**5a**) with Pb(OAc)₄ gave the quinone (**6**) [75%, m.p. 137–139 °C, ¹H n.m.r., CDCl₃, 80 MHz, δ 2.32 (6H,s), 3.72 (6H,s), 6.87 (2H,s), 6.97 (2H,d), 7.45 (2H,d)]. This quinone was reduced without further purification with Zn and acetic acid to give the hydroquinone (**5b**)[‡] (86%, m.p. 191–192 °C). Alkylation with MeI and base yielded 3,3''-dibromo-2,2',5',2''-tetramethoxy-5,5''-dimethyl-[1,1':3',1''-terphenyl] (**5c**)[‡] [94%, m.p. 94–96 °C, ¹H n.m.r., CDCl₃, 80 MHz, δ 2.31 (6H,s), 3.19 (3H,s), 3.59 (6H,s), 3.80 (3H,s), 6.88 (2H,s), 7.13 (2H,d), 7.37 (2H,d)].

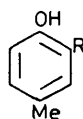
In a second route (**5a**) was alkylated with MeI and base to give (**5d**)[‡] (97%, m.p. 152–153 °C). The nitro group was reduced with magnesium amalgam and TiCl₄⁶ in tetrahydrofuran (THF) to give (**5e**)[‡] (87%, m.p. 225–226 °C) which *via* diazotization in acetic acid was converted into 3,3''-dibromo-2,2',2''-trimethoxy-5,5''-dimethyl-[1,1':3',1''-terphenyl] (**5f**)[‡] [50%, m.p. 144–145 °C, ¹H n.m.r., CDCl₃, 80 MHz, δ 2.32 (6H,s), 3.25 (3H,s), 3.55 (6H,s), 7.13 (2H,d), 7.29 (ABq,3H), 7.38 (2H,d)].

[†] 1 kcal = 4.184 kJ.

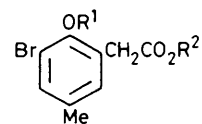
[‡] All new compounds gave satisfactory elemental analyses (C, H, N, \pm 0.3%).



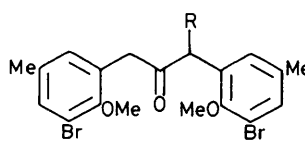
- (1) **a**; R = Me, R¹ = OMe, MX = LiFeCl₄
b; R = Me, R¹ = OMe, MX = LiCl
c; R = Me, R¹ = H, MX = LiFeCl₄
d; R = Me, R¹ = H, MX = LiCl



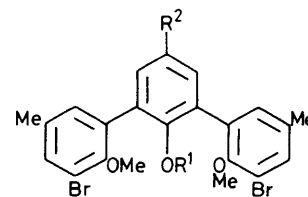
- (2) **a**; R = CO₂Me
b; R = CH₂CO₂H



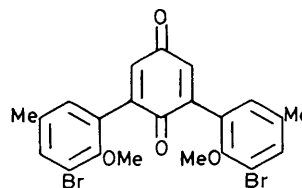
- (3) **a**; R¹ = R² = H
b; R¹ = H, R² = Et
c; R¹ = Me, R² = Et



- (4) **a**; R = CO₂Et
b; R = H



- (5) **a**; R¹ = H, R² = NO₂
b; R¹ = H, R² = OH
c; R¹ = Me, R² = OMe
d; R¹ = Me, R² = NO₂
e; R¹ = Me, R² = NH₂
f; R¹ = Me, R² = H



(6)

Dimetallation of (**5c**) and (**5f**) with BuⁿLi and Bu^sLi respectively in THF at -78 °C gave the dilithiocompounds which were subsequently coupled by reaction with iron(III)

acetylacetonate^{7,8} in benzene. After hydrolysis of the reaction mixture (2 M HCl, FeCl₃) the spherands (**1a**)[‡] and (**1c**)[‡] were isolated in yields of 10–12%. Anion exchange to give (**1b**)[‡] and (**1d**)[‡] was performed by washing CH₂Cl₂ solutions of (**1a**) or (**1c**) with a saturated ethylenediaminetetra-acetic acid solution and a LiCl solution. The ¹H n.m.r. spectra (CDCl₃) of (**1b**) and (**1d**) were consistent with their C_{2h} structures [¹H n.m.r., CDCl₃, 80 MHz, (**1b**) δ 2.50 (12H,s), 3.06 (6H,s), 3.08 (12H,s), 3.93 (6H,s), 7.05 (4H,s), 7.34 (8H,s); (**1d**) δ 2.51 (12H,s), 3.06 (12H,s), 3.10 (6H,s), 7.36 (8H,s), 7.52 (6H, ABq, Δv 3.98, J 3.78 Hz)].

The spherands synthesized differ from those previously reported by Cram and co-workers in the functionalisation of the outer sphere.

We thank the Dutch Kidney Foundation Fund and the Netherlands Foundation for Technical Research (STW), Future Technical Science Branch/Division of the Netherlands

Organization for the Advancement of Pure Research (ZWO), for support of these investigations.

Received, 23rd August 1984; Com. 1215

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