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Benzyltrimethylammonium dichloroiodate (BTMA·ICl₂) is recommended as a new iodinating reagent for the phenolic units in calix[4]arenes. Using a mercury salt method for the iodination of calix[4]arenes with free phenolic units the formation of quinones was observed as a side reaction.

Introduction

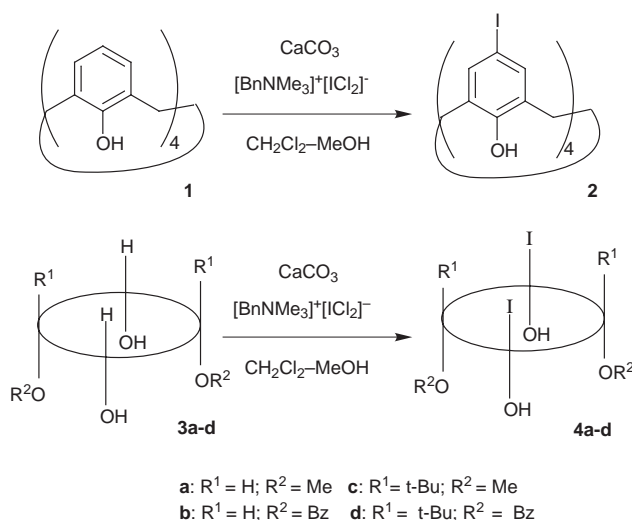
Functionalized calixarenes and especially calix[4]arenes have attracted considerable interest as building blocks for the construction of highly selective host molecules.² Lower rim functionalization can be achieved quite easily by etherification or esterification of the phenolic OH groups, whereas upper rim functionalized compounds can be obtained either directly (electrophilic substitution reactions, Claisen rearrangement) or in a two-step procedure from suitably substituted precursors.³ Halogenated calix[4]arenes^{4,5} are especially useful for this purpose. In this paper we report a very convenient and direct access to iodinated calix[4]arenes.

Results and discussion

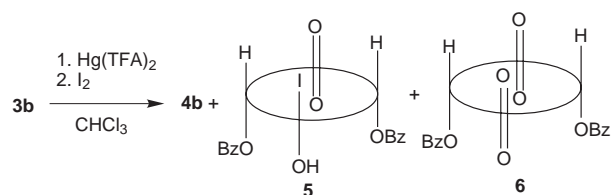
Although iodinations of various calix[4]arenes using metal salts like silver, mercury or thallium trifluoroacetates have been reported in the literature,⁵ iodination of calixarenes bearing free phenolic OH groups seems to be difficult.^{4a,5b} Additionally, working up of the reaction mixtures may cause problems because of the presence of metal iodides and the low solubility of the iodinated compounds. Therefore a reagent is needed which does not suffer from these drawbacks. We found that benzyltrimethylammonium dichloroiodate (BTMA·ICl₂)⁶ is especially suitable for iodinating calix[4]arenes with free phenolic units. It is a stable crystalline compound, which can be employed stoichiometrically and allows the modification of the strength of the iodinating species by variation of the solvent and the auxiliary base. A mixture of methanol (30–40% by volume) and dichloromethane was used as solvent taking care that no crystallization occurs. Calcium carbonate turned out to be the base of choice. The iodinated calixarenes were not formed when potassium carbonate, sodium bicarbonate or potassium bicarbonate were used. The reason for this specific base effect remains unclear.

Utilizing BTMA·ICl₂ it was possible to prepare **2** (Scheme 1) in 63% yield as an analytically pure substance.⁷ Additionally, selective iodination of **3a,b** (to **4a,b**) could be achieved, because BTMA·ICl₂ iodinates only the phenolic parts of the molecule. In general iodination of **3a–d** afforded **4a–d** in 70–80% yield. As can be inferred from the ¹H NMR spectra all iodinated compounds (**2**, **4a–d**) adopt a cone conformation exclusively at room temperature.

Application of the mercury salt method⁸ gave only 40–55% yield of the desired products together with at least three other products. Two of these byproducts could be isolated during iodination of the dibenzoate **3b** (Scheme 2). They were identified as calixquinones **5** and **6**⁹ because of their characteristic C–O stretch frequency at 1655 cm⁻¹ and the ¹³C absorption of



Scheme 1



Scheme 2

the carbonyl carbons in the region of 185 ppm. Although quinones are well known in the calix[4]arene series^{5a,10} to the best of our knowledge they have never been prepared from halogenated calixarenes nor mentioned as byproducts in halogenation reactions. On the other hand the transformation of *p*-halogenated phenols into quinones is known to proceed in high yields (80–90%) when thallium(III) trifluoroacetate is used as the oxidizing agent.¹¹ One can expect that mercury(II) trifluoroacetate can act in a similar manner.

In conclusion we found that calix[4]arenes with free phenolic OH-groups are iodinated in good yields by use of an interhalogen salt, benzyltrimethylammonium dichloroiodate, whereas due to oxidation reactions, quinones can occur as byproducts when metal salt methods are used.¹²

Experimental

General

All solvents were dried referring to usual methods. All com-

mercially available reagents were used without further purification. ^1H NMR spectra were recorded at 300 and 500 MHz, ^{13}C NMR spectra at 75 and 125 MHz. Chemical shifts (δ) were expressed in ppm relative to TMS. Mass spectra were recorded in the CI (isobutane) or EI mode. IR spectra were taken from potassium bromide pellets. Melting points are uncorrected. Analytical thin layer chromatography was performed on pre-coated silica gel plates (Macherey, SIL G/UV₂₅₄), and column chromatography was performed with silica gel (Baker, 40–63 μm). Radial chromatography was performed with silica gel (Merck, PF254) coated plates on a chromatotron (Harrison Associates). Compounds **1**,¹³ **3a**,^{5a} **3b**,¹⁴ **3c**,^{5a} **3d**,¹⁵ and BTMA·ICl₂⁶ were synthesized according to literature procedures.

5,11,17,23-Tetraiodo-25,26,27,28-tetrahydroxycalix[4]arene 2

A solution of **1** (300 mg, 0.708 mmol) and benzyltrimethylammonium dichloroiodate (1.05 g, 3.03 mmol) in CH_2Cl_2 (30 mL) was stirred for 30 min at room temperature, treated with MeOH (12 mL), stirred for 30 min, treated with CaCO_3 (570 mg, 5.70 mmol) and stirred for 24 h at room temperature. After the addition of HCl (conc., 2 mL) and MeOH (60 mL) the orange-red suspension was decolourized with NaHSO_3 (5%, 40 mL) and filtered. The residue was washed with water (10 mL), MeOH (10 mL) and CH_2Cl_2 (40 mL) to afford **2** as a white solid, yield 63%, 315 °C (decomp., violet vapour); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3420, 3157, 1630, 1600, 1465, 1450, 1264, 1206; δ_{H} (300 MHz; $[\text{D}_6]\text{DMSO}$) 7.46 (s, 8H), 4.1–3.1 (m, 12H); δ_{C} (75 MHz; $[\text{D}_6]\text{DMSO}$) 151.4 (s), 136.7 (d), 131.5 (s), 82.8 (s), 29.8 (t); MS (EI) m/z 928 (M^+).

General method for the iodination of compounds 3a–d with BTMA·ICl₂

A solution of **3** (0.40 mmol) and benzyltrimethylammonium dichloroiodate (305 mg, 0.88 mmol) in CH_2Cl_2 (20 mL) was stirred for 30 min at room temperature, treated with MeOH (6–8 mL), stirred for 30 min, treated with CaCO_3 (200 mg, 2.00 mmol) and stirred for 24 h at room temperature. The reaction was quenched by the addition of HCl (conc., 1 mL) and the clear red solution was decolourized with NaHSO_3 (10%, 10 mL). The organic layer was separated, washed three times with water (10 mL), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by column chromatography using CH_2Cl_2 as eluent.

a) **5,17-Diiodo-25,27-dimethoxy-26,28-dihydroxycalix[4]arene 4a**. A white solid, yield 71%, mp >340 °C (>300 °C decomp.),⁸ $R_f(\text{CH}_2\text{Cl}_2) = 0.62$.

b) **5,17-Diiodo-25,27-bis(benzoyloxy)-26,28-dihydroxycalix[4]arene 4b**. A white solid, yield 75%, mp 286–288 °C (decomp.), $R_f(\text{CH}_2\text{Cl}_2) = 0.52$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3547, 1734, 1598, 1584, 1458, 1267, 1175, 1083, 1057, 1023, 709; δ_{H} (500 MHz; CDCl_3) 8.26 (m, 4 H), 7.77 (m, 2 H), 7.64 (m, 4 H), 7.30 (s, 4 H), 7.06–6.88 (m, 6 H), 5.30 (s, 2 H), 3.84 (d, 4 H), 3.51 (d, 4 H); δ_{C} (125 MHz; CDCl_3) 164.6 (s), 152.8 (s), 145.9 (s), 137.5 (d), 134.0 (d), 131.9 (s), 130.5 (d), 130.3 (s), 130.4 (d), 129.6 (2 d), 129.4 (d), 129.2 (d), 128.5 (s), 126.8 (d), 109.5 (s), 82.1 (s), 32.8 (t); MS (EI) m/z 884 (M^+), 105 (COPh).

c) **5,17-Di-tert-butyl-11,23-diiodo-25,27-dihydroxy-26,28-dimethoxycalix[4]arene 4c**. A pale yellow solid, yield 80%, mp >340 °C (>330 °C),⁸ $R_f(\text{CH}_2\text{Cl}_2) = 0.48$.

d) **5,17-Di-tert-butyl-11,23-diiodo-25,27-dihydroxy-26,28-bis(benzoyloxy)calix[4]arene 4d**. A pale yellow solid, yield 82%, mp >340 °C, $R_f(\text{CH}_2\text{Cl}_2) = 0.37$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3510, 2954, 1719, 1654, 1465, 1270, 1180, 706; δ_{H} (300 MHz; CDCl_3) 8.02 (m, 4 H), 7.74 (m, 6 H), 7.16 (s, 4 H), 7.08 (s, 4 H), 4.74 (s, 2 H), 3.69 (d, 4 H), 3.60 (d, 4 H), 1.20 (s, 18 H); δ_{C} (75 MHz; CDCl_3)

164.5 (s), 153.2 (s), 149.4 (s), 145.2 (s), 137.8 (d), 133.8 (d), 132.1 (s), 130.5 (d), 130.1 (s), 129.6 (d), 128.6 (s), 127.0 (d), 81.9 (s), 35.1 (t), 34.4 (s), 31.4 (q); MS (EI) m/z 996 (M^+), 105 (COPh).

Iodination of compound 3b via the mercury salt method

After stirring for 21 h at room temperature a solution of mercury(II) trifluoroacetate (270 mg, 0.63 mmol) and **3b** (200 mg, 0.32 mmol) in CHCl_3 (30 mL) was treated with iodine (160 mg, 0.63 mmol) and stirred for a further 3 h at room temperature. The yellow suspension was filtered, the residue was rinsed with CHCl_3 (30 mL), and the filtrate was washed with $\text{Na}_2\text{S}_2\text{O}_3$ (10%, 20 mL) and three times with water (20 mL). The organic layer was dried over Na_2SO_4 , evaporated to dryness, and purified by radial chromatography using CH_2Cl_2 as eluent.

5,17-Diiodo-25,27-bis(benzoyloxy)-26,28-dihydroxycalix[4]arene 4b. A white solid, yield 55%.

5-Iodo-17,26-dioxo-25,27-bis(benzoyloxy)-28-hydroxy-17,26-dihydrocalix[4]arene 5. A yellow solid, yield 10%, mp >340 °C decomp., $R_f(\text{SiO}_2, \text{CH}_2\text{Cl}_2) = 0.14$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3522, 1720, 1658, 1458, 1268, 710; δ_{H} (500 MHz; CDCl_3) 8.30 (m, 4 H), 7.78 (m, 2 H), 7.64 (m, 4 H), 7.28 (s, 2 H), 7.04 (d, AB₂, 2 H), 7.00 (d, AB₂, 2 H), 6.95 (t, AB₂, 2 H), 6.41 (s, 2 H), 4.98 (s, 1 H, OH), 3.81 (d, 2H), 3.64 (d, 2 H), 3.52 (d, 2 H), 3.39 (d, 2 H); δ_{C} (125 MHz; CDCl_3) 187.6 (s), 185.8 (s), 164.6 (s), 153.0 (s), 147.3 (s), 146.9 (s), 137.5 (d), 134.2 (d), 132.9 (d), 132.1 (s), 130.9 (s), 130.6 (d), 129.3 (d), 130.2 (d), 129.8 (d), 129.6 (s), 128.7 (s), 126.2 (d), 82.7 (s), 33.0 (t); MS (EI) m/z 772 (M^+), 105 (PhCO).

5,17,26,28-Tetraoxo-25,27-bis(benzoyloxy)-5,17,26,28-tetrahydrocalix[4]arene 6. A pale yellow solid, yield 3%, mp 278–282 °C (decomp.), $R_f(\text{SiO}_2, \text{CH}_2\text{Cl}_2) = 0.05$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1732, 1655, 1266, 710; δ_{H} (300 MHz; CDCl_3) 8.27 (m, 4 H), 7.78 (m, 2 H), 7.61 (m, 4 H), 7.08 (m, 4 H), 6.96 (m, 2 H), 6.37 (br s, 4 H), 3.6–3.4 (br s, 8 H, ArCH₂Ar); MS (EI) m/z 660 (M^+), 105 (COPh).

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