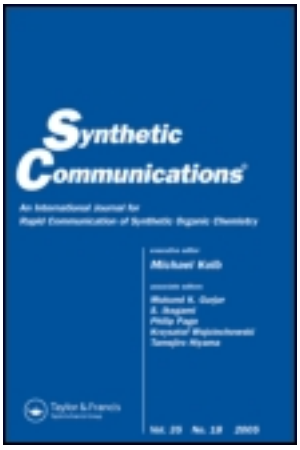


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Selective Mono-Dealkylation of Tetra-p-tert-butyl-calix[4]arene at the Upper Rim

Sandrine Berthalon [a] , Jean-Bernard Regnouf deVains [a] & Roger Lamartine [a]

[a] Reconnaissance et Organisation Moléculaire et Biomoléculaire, UPRES A du CNRS, Laboratoire de Chimie Industrielle, Université Claude Bernard, 69622, Villeurbanne, France

Version of record first published: 21 Aug 2006

To cite this article: Sandrine Berthalon, Jean-Bernard Regnouf deVains & Roger Lamartine (1996): Selective Mono-Dealkylation of Tetra-p-tert-butyl-calix[4]arene at the Upper Rim, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:16, 3103-3108

To link to this article: http://dx.doi.org/10.1080/00397919608004615

SYNTHETIC COMMUNICATIONS, 26(16), 3103-3108 (1996)

SELECTIVE MONO-DEALKYLATION OF TETRA-*p*-*tert*-BUTYL-CALIX[4]ARENE AT THE UPPER RIM.

Sandrine Berthalon, Jean-Bernard Regnouf de Vains*, Roger Lamartine.

Reconnaissance et Organisation Moléculaire et Biomoléculaire, UPRES A du CNRS, Laboratoire de Chimie Industrielle, Université Claude Bernard, 69622 Villeurbanne, France.

Abstract : The tris-p-(tert-butyl)calix[4]arene has been synthesized by a reproducible selective esterification-dealkylation-saponification process.

In the field of supramolecular chemistry, the *p-tert*-butyl-calix[4]arene plays a fundamental role, with regards to its complexing properties and controlled functionalization abilities. Many reviews have focused on this family of phenolic cyclic oligomers[1], revealing in some cases interesting industrial behaviour[2]. Their thermal and chemical stabilities associated with their complexing properties render them good candidates for these last purposes, even under drastic conditions.

The selective functionalization of upper and lower rims has been widely studied during the last twenty years[1] but surprisingly only a few papers are relating the introduction of a single active group on the upper rim. For this purpose, the fully de-*tert*-butylated calix[4]arene protected with stable or labile protective groups (ethers or esters) is generally used as starting material such as in the synthesis of its mono-*p*-allyl[3], mono-*p*-nitro[4] and mono-*p*-formyl[5] derivatives.

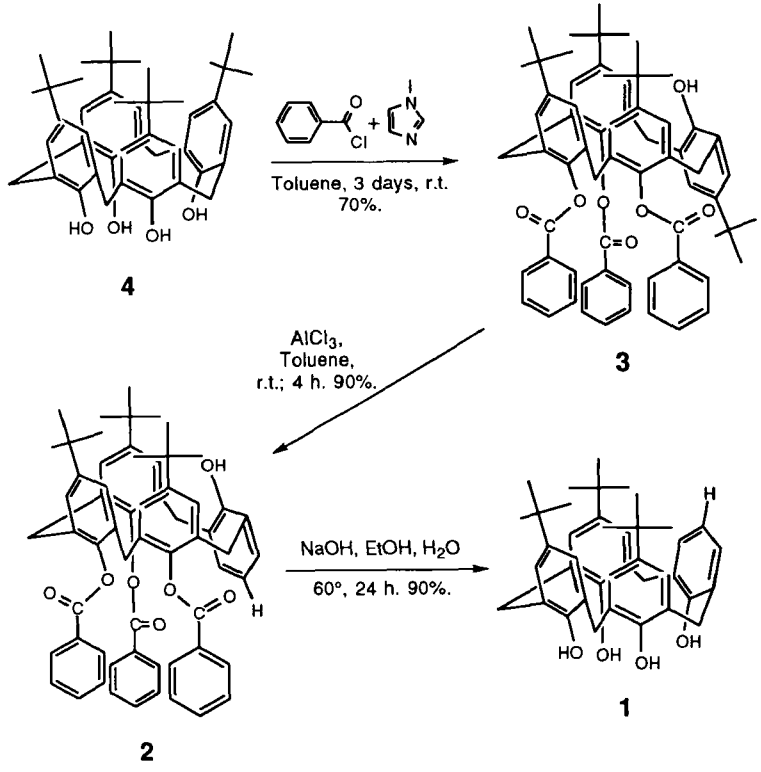
In this field, we were interested in a large scale synthesis of the 5,11,17-tri-*p-tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene **1**, our synthetic strategy being directed by two main principles: 1) keeping as far as possible the *p-tert*-butyl-calix

*To whom correspondence should be addressed.

[4]arene identity through its cone conformation, its lower-rim hydrogen bonds crown and its lipophilic cone-like head; 2) using the most simple pathways in view of large-scale synthesis and industrial applications.

Gutsche et al.[6] developed for a conic analogue of **2** a synthetic pathway consisting in the 3,5-dinitrobenzoylation in MeCN, in the presence of the weak nucleophile N-methyl imidazole, of three of the -OH groups of the tetra-*p-tert*-butyl-calix[4]arene **4** followed by the *retro Friedel and Craft* dealkylation of the unprotected phenol. We met in fact a lot of difficulties to reproduce the tri-esterification step and found surprisingly that this analogue of **2** has not been, until now and as far as we know, used in the synthesis of **1**.

We tried in parallel to remove selectively the *tert*-butyl group by a stœchiometric retro-*Friedel and Craft* reaction on **4**, but this experiment afforded a mixture of compounds which were analyzed as the successive *de*-tertbutylation products[7].



Thus, reacting in toluene over a three days period and at r.t. the calix[4]arene **4** with benzoyl chloride in the presence of N-methyl imidazole afforded **3** in a 70% yield process. The reaction was TLC monitored (SiO_2, CH_2Cl_2/hexane) and necessitated regular addition of acid chloride and base.The following smooth de-*tert*-butylation of **3** was carried out with $AlCl_3$ in toluene at r.t. yielding **2** as a colourless compound (90%). Finally, the three ester functions were hydrolysed with NaOH in a water / ethanol medium over a 24 h period. The resulting tri-*tert*-butylcalix[4]arene **1** was obtained in a 90% yield process. Compounds **3**, **2** and **1** were precipitated pure by cold evaporation of CH_2Cl_2 from CH_2Cl_2/MeCN or CH_2Cl_2/MeOH solutions of their raw organic mixtures.

Table: ^{1}H-NMR conformationnal analysis of **3**, **2** and **1**.

	Ar-C*H*$_2$-Ar (ppm, Hz)	Ar-C*H*$_2$-Ar (ppm, Hz)	conformation
3	AB 3.45-4.16 J_{AB} = 13.5 AB 3.80-4.00 J_{AB} = 16.5	33.12 39.71	*syn-syn-syn* partial cone
2	AB 3.50-4.14 J_{AB} = 13.5 AB 3.81-4.03 J_{AB} = 16.5	33.12 39.68	*syn-syn-syn* partial cone
1	AB 3.50-4.25 J_{AB} = 12.5	32.35 32.59	cone

As shown in Table, the ^{1}H and ^{13}C NMR analyses demonstrated, according to *de Mendoza et al.* [8], that the steric hindrance generated by the three benzoate groups in **3** and **2** distorded the calixarene ring from cone to partial cone. It is interesting to note that in **3**, the symmetries of the two AB patterns (Ar-C*H*$_2$-Ar groups) indicate, *a contrario* to its *syn-anti-syn* nitrobenzyl analogue[6], that the inversed phenol ring may be the unprotected one, giving a *syn-syn-syn* partial cone conformation. This observation, confirmed by the three residual *tert*-butyl groups chemical shifts, can also be done for **2**.Recovery of the desired cone conformation was in fact observed in the deprotected dealkylated calixarene **1**. All compounds gave satisfactory analytical results.

EXPERIMENTAL

General: Melting points (°C, uncorrected) were determined on a Electrothermal 9100 Capillary apparatus. ^1H and ^{13}C-NMR spectra were recorded on a Bruker AM 300 (300 MHz) and a Bruker AC 200 (50.3 MHz) respectively ($CDCl_3$, TMS as internal standard, chemical shifts in ppm). Mass spectra were obtained by electrospray technique (HP 5989/MS Engine, Service Central d'Analyse, CNRS, Solaize). Infra-red was performed on a Mattson 5000 FT apparatus (ν in cm^{-1}) and UV spectra were recorded on a Perkin-Elmer Lambda 2 UV/VIS apparatus (λ max in nm, ε in $mol^{-1}\,l\,cm^{-1}$). Elemental analyses were performed at the Service Central de Microanalyse, Ecole Supérieure de Chimie, Montpellier. Macherey-Nagel TLC plates were used for chromatography analysis (SiO_2, Polygram SIL G/UV254, ref.805021). All commercialy available products were used without further purification unless specified otherwise.

Tribenzoate 3: To a solution of tetra-*p-tert*-butylcalix[4]arene **4** (toluene complex[8], 1.6g, 2.15 mmol) in 100 ml of dry toluene were added N-methylimidazole (1 ml, 12.5 mmol) followed by benzoyl chloride (0.8 ml, 6.9 mmol). The resulting precipitate was immediatly dissolved by a rapid heat-gun heating and the solution was stirred at r.t. during 24 h. N-methylimidazole (0.35 ml, 4.3 mmol) and benzoyl chloride (0.25 ml, 2.15 mmol) were then added and stirring was continued for 24 h. This operation was renewed one time. Cold water (100 ml) was added and the mixture was vigourously stirred during 1 h. The organic phase was recovered, washed with cold water (3 x 25 ml), dried over Na_2SO_4 and evaporated to dryness. Trituration of the residue with CH3CN afforded **3** as a white powder (1.5 g; 70%).Mp: 335-336°C. IR: 1730 (strong, C=O). UV: 277 (7200). ^1H-NMR: 0.68 (s, 2 Me_3C); 0.81 (s, Me_3C); 1.40 (s, Me_3C); 3.45, 4.16 (AB, J_{AB} = 13.5, 2 Ar-CH_2-Ar); 3.80, 4.00 (AB, J_{AB} = 16.5, 2 Ar-CH_2-Ar); 6.45-6.65 (m, 7H); 6.85-6.98 (m, 4H); 7.1-7.28 (m, 6H of Ar); 7.50 (t, J = 7.5, 2H of benzoyl); 8.05 (d, J = 7.2, 4H of benzoyl). ^{13}C-NMR: 31.43 (Me_3C); 31.69 (Me_3C); 32.58 (Me_3C); 33.12 (Ar-CH_2-Ar); 34.45, 34.58 and 34.92 (Me$_3C$); 38.71 (Ar-CH_2-Ar); 126.31, 126.82, 127.32, 128.64, 129.84, 130.72, 131.09, 133.27 and 133.86 (aromatic *C* -(H)); 129.15, 130.18, 132.49, 132.81, 133.31, 143.67, 144.85, 146.70, 148.77, 149.30, 150.75 and 154.75 (aromatic *C* -(O) and *C* -(C)); 154.01 and 165.70 (*C* = O). Analysis *calc. for* $C_{65}H_{68}O_7$ (961.26): C 81.22, H 7.13, O 11.65; *found*: C 80.98, H 7.20, O

11.72. ES-MS: 983.6 ([M-H + Na]$^+$); 863.6 ([M-H -C_6H_5COO+ Na]$^+$); 743.6 ([M-H -2 (C_6H_5COO)+ Na$^+$]).

Tribenzoate 2: tribenzoate **3** (2 g; 2,1 mmol) was added to a suspension of $AlCl_3$ in dry toluene (7.8 g, 58 mmol ; 150 ml) under N_2. The mixture was warmed with a heat-gun during 5 min then stirred at r.t.. After 4 h, the mixture was treated under vigourous stirring with 1N HCL (50 ml) during 1 h. After separation, the acidic phase was washed with $CHCl_3$ (3 x 25 ml) and the combined organic phases were dried over Na_2SO_4 then evaporated to dryness. The resulting residue was triturated with CH_3CN affording **2** as a white powder (1.7 g; 70%).Mp: 293.6-295.6°C. IR: 1730 (strong, C=O). UV($CHCl_3$): 284 (s, 7500); 275 (8900). ^{1}H-NMR: 0.71 (s, 2 (Me_3C); 0.83 (s, Me_3C); 3.50, 4.14 (AB, J_{AB} = 13.6, 2 Ar-CH_2-Ar); 3.81, 4.03 (AB, J_{AB} = 16.5, 2 Ar-CH_2-Ar); 6.50-6.70 (m, 7H); 6.85-7.00 (m, 5H); 7.10-7.29 (m, 7H); 7.53 (t, J = 7.45, 2H of benzoyl); 8.03 (d, J = 7.2, 4H of benzoyl). ^{13}C-NMR: 31.49 (Me_3C); 31.69 (Me_3C); 33.12 (Ar-CH_2-Ar); 34.49 (Me$_3$*C*); 39.68 (Ar-CH_2-Ar); 121.10, 126.50, 126.85, 127.35, 128.69, 129.60, 129.83, 130.73, 131.09 and 133.87. (aromatic *C* -(H)); 129.05, 130.13, 132.18, 132.85, 133.32, 133.51, 145.08, 148.50, 149.39, 153.31 (aromatic *C* -(O) and *C* -(C)); 164.00 and 165.65 (C = O). Analysis *calc. for* $C_{61}H_{59}O_7$ (904.15): C 81.04, H 6.58, O 12.39; *found*: C 80.87, H 6.79, O 12.51. ES-MS: 927.6 [M + Na]$^+$; 905.5 [M+H]$^+$.

Tri-*p-tert*-butyl-calix[4]arene 1: A mixture of **2** (0.5g, 0.55 mmol), NaOH (2 g, 50 mmol), EtOH (20 ml) and H_2O (20 ml) was heated at 60°C during 24 h then acidified with HCl 2N until the formation of a precipitate was complete. After vigourous stirring (1 h), the resulting suspension was extracted with $CHCl_3$ (2 x 100 ml). The organic phases were combined, dried over Na_2SO_4 then evaporated to dryness. The residue was triturated with MeOH (30 ml) affording **1** as a white powder (0.29 g; 90%).Mp: 324-325°C (dec). IR: no C=O band. UV: ($CHCl_3$): 278 (10200); 287 (s, 7900). ^{1}H-NMR: 1.21 (s, Me_3C); 1.24 (s, 2 Me_3C); 3.50, 4.25 (*br* AB, J_{AB} = 12.5, 4 Ar-CH_2-Ar); 6.74 (t, J = 7.5, 1 H); 6.90-7.15 (m, 8H); 10.30 (s, 4 O*H*). ^{13}C-NMR: 31.48 (Me_3C); 31.54 (Me_3C); 32.35 (Ar-CH_2-Ar); 32.59 (Ar-CH_2-Ar); 34.14 (Me$_3$*C*); ; 122.42, 125.95, 126.16, 126.31 and 129.22 (aromatic *C* -(H)); 127.42, 127.77, 128.02, 128.66, 144.60, 146.37, 146.78 and 149.08 (aromatic *C* -(O) and *C* -(C)). Analysis *calc. for* $C_{40}H_{48}O_4$ (592.83): C 81.04, H 8.16, O 10.79; *found*: C 81.30, H 8.11, O 10.45. ES-MS: 615.6 ([M + Na]$^+$); 593.6 ([M+H]$^+$); 537.5 ([M - (*tert*-Bu) + H]$^+$); 481.4 ([M - 2 (*tert*-Bu) + H]$^+$); 425.3 ([M - 3 (*tert*-Bu) + H]$^+$).

REFERENCES

1. a) Gutsche, C. D. "Calixarenes", Monographs in Supramolecular Chemistry, Series Ed. Stoddart, J. F. Royal Society of Chemistry, Cambridge, 1989. b) "Calixarenes. A Versatile Class of Macrocyclic Compounds.", Eds. Vicens J. and Böhmer V., Kluwer Academic Publishers, Dordrecht, 1991. c) Shinkai, S. "Calixarene as the Third Supramolecular Host", in Advances in Supramolecular Chemistry, Vol 3, pp 97-130, Ed. Gokel, G.W. J. Press Inc, 1993. d) " Calixarenes 50th Anniversary: Commemorative Volume", Eds. Vicens J., Asfari Z. and Harrowfield J. McB, Kluwer Academic Publishers, Dordrecht, 1994. e) "Calixarenes, Macrocycles with (Almost) Unlimited Possibilities.", Böhmer, V. *Angew. Chem..Int. Ed. English* **1995**, *34*, 713.
2. Perrin, R.; Lamartine, R.; Perrin, M. *Pure and Appl. Chem.* **1993**, *7*, 1549.
3. Gutsche, C. D.; Lin, L. *Tetrahedron* **1986**,*42*(6),1633.
4. Nam, C.K.; Kim, D.S. *Bull. Korean Chem. Soc.* **1994**, *15*(4), 284.
5. Arduini, A.; Manfredi, G.; Pochini, A.; Sicuri, A.R.; Ungaro, R. *J.Chem.Soc., Chem. Commun.* **1991**, 936.
6. See, K.A.; Fronczek, F.R.; Watson, W.H.; Kashyap, R.P.; Gutsche, C. D. *J. Org. Chem.* **1991**, *56*, 7256.
7. Regnouf de Vains, J.-B.; Hayat, U., unpublished results
8. Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P.M.; Sanchez, C. *J. Org. Chem.* **1991**, *56*, 3372.

(Received in The Netherlands 01 March 1996)