

Microwave-assisted alkylation of *p*-*tert*-butylcalix[4]arene lower rim: the effect of alkyl halides

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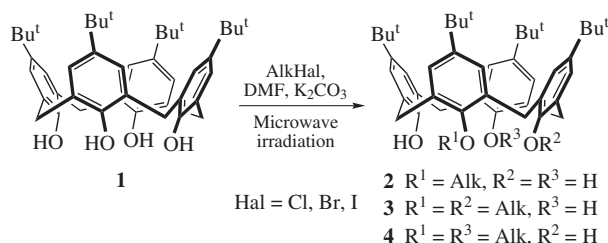
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DOI: 10.1016/j.mencom.2013.03.022

Alkylation of *p*-*tert*-butylcalix[4]arenes with alkyl bromides or iodides under microwave irradiation affords mostly the corresponding distal disubstituted ethers, whereas in case of alkyl chlorides reasonable yields of monoethers were achieved.

Calix[4]arenes^{1,2} are generally obtained by condensation between formaldehyde and phenols. Their unique properties are due to their cavity and can be tuned by functionalization of their upper and lower rim.^{3–8} Calix[4]arenes find use in supramolecular chemistry as macrocyclic receptors, sensors and components of molecular devices.^{9–13} One of the main problems in calixarene functionalization is a long reaction time and low yields of products. Microwave irradiation is widely used to accelerate reactions,^{14–19} which seems reasonable to be extended into calixarene chemistry.

In the present work, O-alkylation of *p*-*tert*-butylcalix[4]arene **1** with haloalkanes under microwave irradiation (Scheme 1) was studied, halogen, length of alkyl chain and nature of phase-transfer catalyst having been varied.



Firstly, halogen nature influence on the etherification outcome was tested using BuHal (Hal = Cl, Br, I) as a model reactant. Reaction course was controlled by TLC, MALDI-TOF spectrometry and ¹H NMR spectroscopy. In all cases formation of three products was established, which were monosubstituted (**2**), proximal (**3**) and distal (**4**) disubstituted derivatives (Table 1). Neither tri- nor tetra-substituted ones were detected. The presence of mono- and diethers (**2–4**) in the reaction mixture can be easily observed in ¹H NMR spectra, in which signals of OH protons are very characteristic. Such protons of proximal and distal disubstituted derivatives appear as singlet at 8.95²⁰ and 7.81²¹ ppm, respectively, whereas two singlets at 9.61 and 10.20 ppm are assigned to OH groups of monoether.²²

Reaction of compound **1** (0.47 mmol) with BuCl (1.2 mmol) in the presence of K₂CO₃ (2.4 mmol) in DMF (1 ml) after 10 min of MW irradiation (400 W) afforded 40% of monoether **2** as a major product.[†] Processing under conventional heating provided 44% yield of monoether after 18 h.²³ The content of distal diether **4** in reaction mixture was small at the beginning and became

Table 1 Ratios of reagents, conditions and products of reaction of *p*-*tert*-butylcalix[4]arene **1** with alkyl halides.

Entry	AlkHal	Time of reaction/min	Mono-substituted ether 2 ^a (%)	Proximal disubstituted ether 3 ^a (%)	Distal disubstituted ether 4 ^a (%)	1 :AlkHal ratio	TBAB
1	BuCl	10	40	0	6	1:2.5	–
2	BuCl	20	41	6	32	1:2.5	–
3	BuCl	40	33	5	33	1:2.5	–
4	BuCl	40	52	0	11	1:2.5	+
5	BuCl	80	22	7	48	1:2.5	–
6	BuCl	100	24	6	44	1:2.5	–
7	BuCl	120	45	3	22	1:4.5	–
8	BuCl	120	51	2	22	1:4.5	+
9	BuBr	10	15	10	67	1:2.5	–
10	BuBr	20	14	10	71	1:2.5	–
11	BuBr	40	7	7	75	1:2.5	–
12	BuBr	40	4	7	76	1:2.5	+
13	BuBr	80	5	2	90	1:2.5	–
14	BuBr	100	5	2	89	1:2.5	–
15	BuBr	120	2	8	84	1:4.5	+
16	BuBr	120	3	9	85	1:4.5	–
17	BuI	10	12	13	73	1:2.5	–
18	BuI	20	23	5	65	1:2.5	–
19	BuI	40	27	4	66	1:2.5	–
20	BuI	40	9	11	77	1:2.5	+
21	BuI	80	4	4	89	1:2.5	–
22	BuI	100	17	4	69	1:2.5	–
23	BuI	120	14	5	76	1:2.5	–
24	BuI	120	1	5	93	1:4.5	+
25	BuI	120	5	5	89	1:4.5	–
26	<i>n</i> -C ₆ H ₁₃ Br	40	5	10	81	1:2.5	–
27	<i>n</i> -C ₈ H ₁₇ Br	40	5	11	82	1:2.5	–
28	<i>n</i> -C ₁₀ H ₂₁ Br	40	14	9	74	1:2.5	–
29	<i>n</i> -C ₁₂ H ₂₅ Br	40	3	10	85	1:2.5	–
30	<i>n</i> -C ₁₄ H ₂₉ Br	40	3	9	87	1:2.5	–
31	<i>n</i> -C ₁₆ H ₃₃ Br	40	7	8	81	1:2.5	–

^a Content in the reaction mixture determined with ¹H NMR spectrometry.