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Copper-Catalysed Allylic Substitution Using 2,8,14,20-Tetrapentylresorcinarenyl-Substituted Imidazolium Salts

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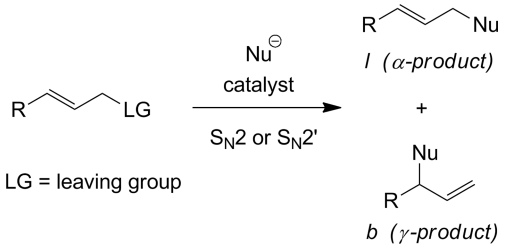
Unsymmetrical imidazolium salts, each having one nitrogen atom (N1) substituted by a cavity-shaped TPR group (TPR = 2,8,14,20-tetrapentylresorcinaren-5-yl), were tested in situ as proligands for the copper-catalysed allylic arylation of cinnamyl bromide with arylmagnesium halides. The catalytic systems produced mixtures of linear (l) and branched (b) arylated compounds in variable proportions, with the b/l ratio being the highest (78:22) for the most crowded imidazolium salt used, namely that in which the second nitrogen atom (N2) was substituted by a mesityl group. An N-heterocyclic carbene complex obtained from one of the imidazolium salts was characterised by an X-ray diffraction study.

Introduction

Allylic substitution, the metal-catalysed reaction between a nucleophile and a substrate containing a leaving group in an allylic position (Scheme 1), is a well-established synthetic procedure of modern organic chemistry.[1–3] Being applicable to the formation of carbon–carbon, carbon–nitrogen, and carbon–oxygen bonds, it has become very popular in the field of natural product synthesis as well as in biomolecular and medicinal chemistry. Regioselectivity is a key issue in this reaction. The nucleophilic attack can lead to two compounds, the S_N2-product (or α-product) or the S_N2'-product (or γ-product), with regiocontrol of the reaction depending on various factors, such as the leaving group, the nature of the solvent, and the catalytic ligand-metal combination.[4] Whereas palladium remains the most frequently employed metal for this reaction, copper-catalysed allylic substitution,[5] which allows the use of Grignard reagents as well as organozinc compounds, has recently emerged as a method that usefully complements palladium catalysis. Interestingly, allylic substitution with this particular metal often proceeds with S_N2'-regioselectivity,[6–11] this being relevant to the synthesis of chiral compounds using an inexpensive and readily available metal.



Scheme 1. Allylic substitution.

We have recently described a series of nickel and palladium complexes containing N-heterocyclic carbene ligands (NHCs) in which one nitrogen atom (termed N1 hereafter) is substituted by a cavity-shaped 2,8,14,20-tetrapentyl resorcin[4]aren-5-yl group (abbreviated TPR). Suzuki–Miyaura (palladium)[12,13] and Kumada–Tamao–Corriu (nickel)[14] cross-coupling studies with these complexes revealed the beneficial role of the flexible pentyl fragments, which, in combination with the rigidity of the cavitand core, can sterically interact with the primary coordination sphere of the metal and thus provide assistance in the reductive elimination step. As such, the TPR group should be considered as a bulky group. Its effective steric bulk in the corresponding carbene complexes is, however, difficult to quantify accurately, particularly because a coordinated metal centre may be positioned either above the cavity entrance or pushed towards its exterior, this leading to different steric effects. As an extension to our studies on complexes with bulky, cavity-shaped ligands, we have now examined the arylation properties of NHC-copper based systems derived from the TPR-substituted imidazolium salts **1**–**4** (Fig-

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ure 1). These imidazolium salts differ only in the substituent attached to the N2 nitrogen atom (benzyl, CH_2(TPR), $CH_2\{(2,6\text{-}OMe)_2C_6H_3\}$, mesityl). The azolium salts were all assessed in situ in the allylic arylation of cinnamyl bromide with arylmagnesium halides. We presumed that all the NHCs generated from these salts would have comparable electronic donor properties and thus only differ in the extent of steric encumbrance. The use of Cu-NHC catalysts in allylic substitution is well documented.[4,6–11]

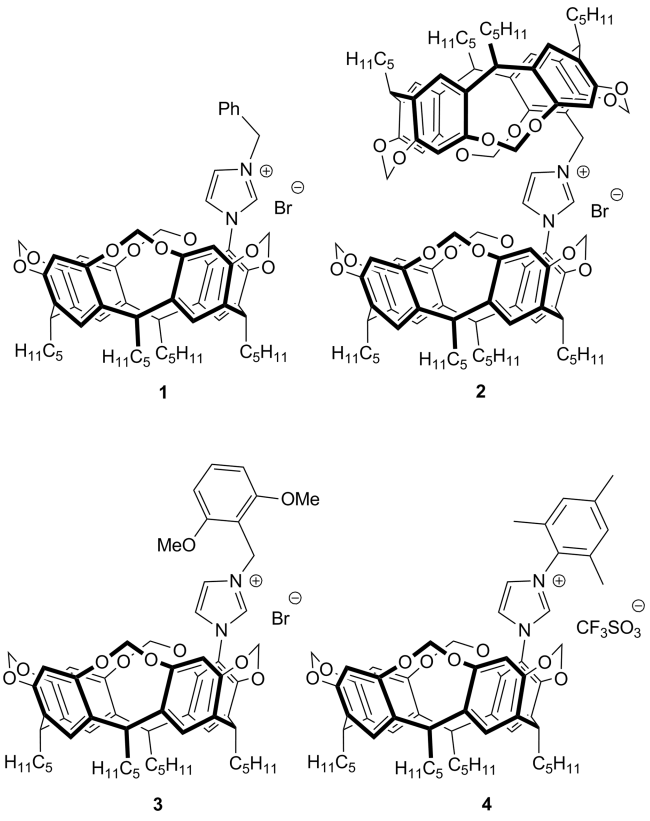
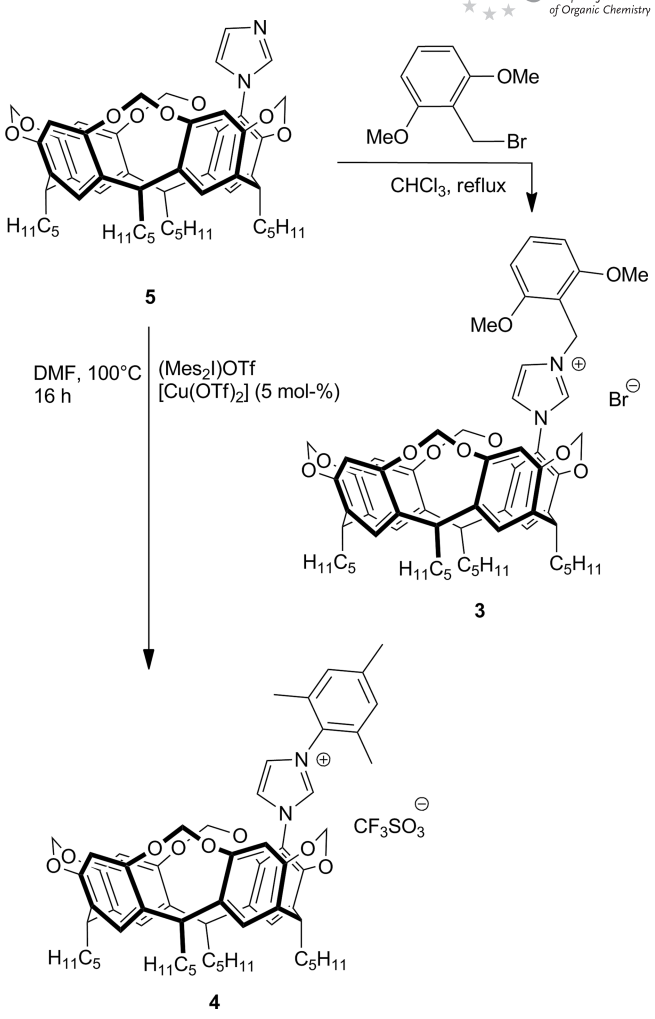


Figure 1. The four TPR-substituted imidazolium salts **1**–**4** used in this study, ranged in order of increasing bulk. TPR stands for tetrapentylresorcinaren-5-yl. Being connected to a nitrogen atom via the C-5 carbon atom, the TPR group does not behave as a substituent with axial symmetry.

Results and Discussion

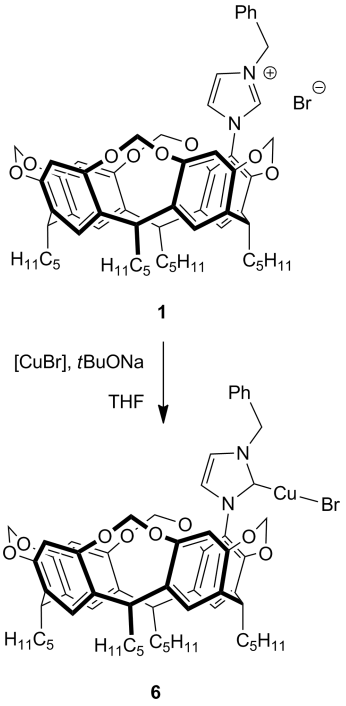
The catalytic systems tested in the present study (see below) were generated in situ by mixing $[Cu(OTf)_2]$ ($OTf^- = CF_3SO_3^-$, triflate) and the corresponding imidazolium salt in Et_2O at room temperature. Imidazolium salts **3** and **4** are new compounds. The former was obtained quantitatively by alkylating *N*-TPR-imidazole (**5**) with 2-bromomethyl-1,3-dimethoxybenzene in refluxing chloroform (Scheme 2). Salt **4** was obtained in 48% yield by reacting **5** with $(Mes_2I)OTf$ in *N*,*N*-dimethylformamide (DMF) at 100 °C for 16 h. Both compounds were characterised by ^1H and ^{13}C NMR spectroscopy, ESI-TOF MS, and elemental analysis (see Experimental Section). Consistent with C_s symmetry of the molecules, the corresponding ^1H NMR spectra each display two AB patterns for the four OCH_2O groups and two triplets for the methine protons.



Scheme 2. Synthesis of imidazolium salts **3** and **4**.

The ease of forming copper carbene complexes with the above salts was demonstrated formally only for **1** (Scheme 3). Thus, when this salt reacted with NaO*t*Bu and CuBr (in 1:1:1 ratio) in tetrahydrofuran (THF), copper(I) complex **6** was formed.[15] In the ^{13}C NMR spectrum, the carbenic carbon atom appears at δ = 135.56 ppm. The structure of **6** was confirmed by an X-ray diffraction study (Figure 2). The core of the resorcin[4]arene shows the classical bowl-shaped structure found in other resorcinarene-derived cavitands[15–18] with separations between opposed pairs of C-2 atoms (the C-2 atoms are the OC*C*CO atoms of the wider rim) of 7.93 and 7.96 Å. Interestingly, in the solid, the CuBr unit is pushed outside the cavity, although positioning of the Cu atom above the cavity could be envisaged from a steric point of view. In the observed configuration, the percent buried volume ($\%V_{bur}$) is 28.8, vs. 36.2 estimated were the carbene to be positioned above the cavity. The interplanar angle between the imidazoylidene unit and the aromatic ring to which it is connected is 85°. The molecule crystallises with two molecules of diethyl ether, one of which is poised at the upper entrance of the cavity.

To assess the catalytic systems, cinnamyl bromide was treated with various arylmagnesium halides (Scheme 4).



Scheme 3. Synthesis of copper complex **6**.

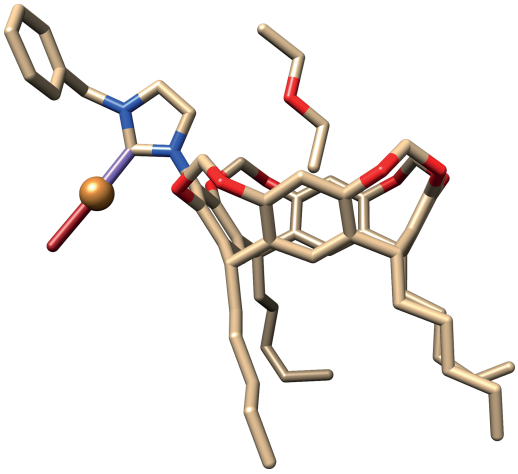
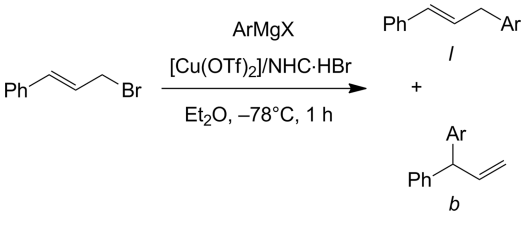


Figure 2. Molecular structure of **6**. A molecule of Et_2O occupies the cavity entrance, another one (not shown for clarity) is remote from the cavity. The interplanar angle between the imidazolylidene unit and the aromatic ring to which it is connected is 85°.



Scheme 4. Copper-catalysed allylic arylation of cinnamyl bromide with an arylmagnesium halide.

The reactions were performed at –78 °C with a cinnamyl bromide/Cu ratio of 100. The conversions were determined by ^{1}H NMR spectroscopic analysis after 1 h reaction time (this period of time including the time of addition of the Grignard reagent).

We began the study by determining whether the time taken for the addition of phenylmagnesium bromide to a solution containing a mixture of cinnamyl bromide, [Cu(OTf)$_2$] and **1**, influenced the catalytic outcome. We observed that irrespective of the duration of addition (1 h, 10 min, or less than 1 min), the substitution reaction was complete 1 h after having started the addition of the Grignard reagent (Table 1). In keeping with previous reports, we also found that the proportion of linear product increased slightly when the Grignard reagent was added rapidly, with its highest value reaching 78% (entries 4).[4] Notably, no significant differences were seen between runs using preformed complex **6** and tests carried out with the catalyst obtained from **1** in situ (entries 1 and 2); this observation justified the use of catalysts generated in situ.

Table 1. Copper-catalysed allylic arylation of cinnamyl bromide with phenylmagnesium bromide: Influence of the time taken for Grignard addition.[a]

Entry	Salt or complex	Addition of PhMgBr	Conversion [%][b]	Linear [%][b]	Branched [%][b]
1	**1**	over 1 h	100	68	32
2	**6**	over 1 h	100	70	30
3	**1**	over 10 min	100	72	28
4	**1**	fast (< 1 min)	100	78	22

[a] Reaction conditions: [Cu(OTf)$_2$] (1 mol-%), imidazolium salt (1 mol-%), PhCH=CHCH$_2$Br (0.32 mmol), PhMgBr (0.39 mmol), Et_2O (3 mL), –78 °C, 1 h. [b] The conversion and the linear/branched product ratios were determined by ^{1}H NMR spectroscopic analysis (accuracy of ± 5%).

Given that the rate of addition had practically no influence on the conversion, all further tests were carried out under fast addition of Grignard reagent, and stopped after 1 h. As described above, each run was performed at –78 °C (Table 2). The proportion of branched product increased in the order **1** < **2** < **3** < **4**, with the b/l ratios varying from 22:78 for **1** to 78:22 for **4** (entries 1–4). Thus, the observed b/l ratios seemingly correlate with the steric bulk of the ligand.[19] Comparison of **2** with two related salts, namely **7** and **8**, in which the TPR group was replaced by a smaller phenyl or calix[4]arenyl substituent, confirmed this trend (Figure 3). Here, the b/l ratios were 20:80 (**7**) and 16:84 (**8**)

Table 2. Copper-catalysed allylic arylation of cinnamyl bromide and phenylmagnesium bromide. Influence of imidazolium salts **1**–**4**, **7** and **8**.[a]

Entry	NHC·HCl	Conversion [%][b]	Branched [%][b]	Linear [%][b]
1	**1**	100	22	78
2	**2**	100	31	69
3	**3**	100	47	53
4	**4**	100	78	22
5	**7**	100	20	80
6	**8**	100	16	84

[a] Reaction conditions: [Cu(OTf)$_2$] (1 mol-%), imidazolium salt (1 mol-%), PhCH=CHCH$_2$Br (0.32 mmol), PhMgBr (0.39 mmol), Et_2O (3 mL), –78 °C, 1 h. [b] The conversion and the linear/branched proportions were determined by ^{1}H NMR spectroscopic analysis (accuracy of ± 5%).

(vs. 31:69 for **2**) (entries 2, 5 and 6). Note also that the proportion of branched product was significantly higher for **2** than for **8**, which is consistent with a TPR group having a greater steric bulk than a calixarenyl group.

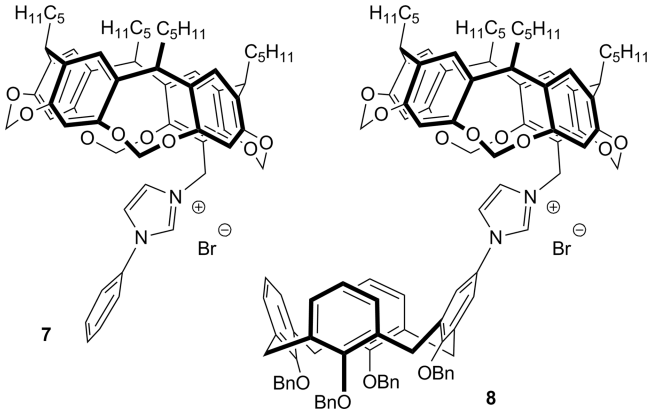


Figure 3. Imidazolium salts **7** and **8**.

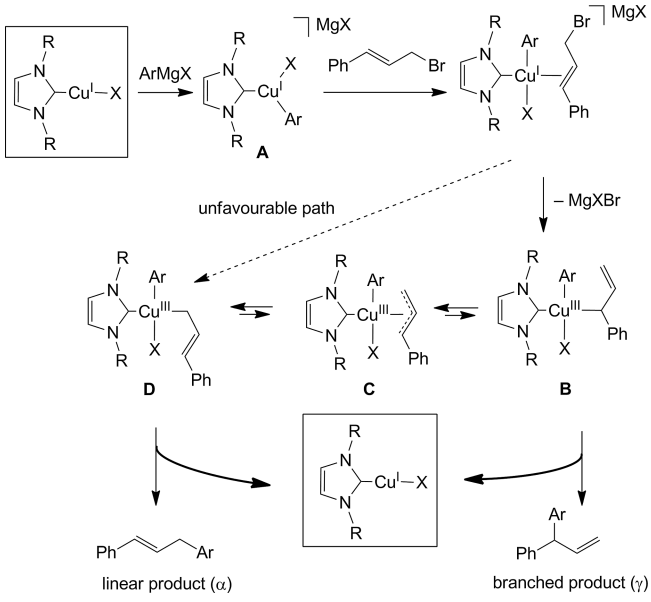
To establish whether the selectivity was dependent upon the nature of substituents on the Grignard reagent, *p*-chlorophenylmagnesium bromide, *p*-fluorophenylmagnesium bromide and *o*-methylphenylmagnesium chloride were tested with the catalytic system [Cu(OTf)$_2$]/**4** (1 mol-% Cu) (Table 3). The reaction rates observed for the two *p*-substituted Grignard reagents were relatively high, and were comparable to those obtained for phenylmagnesium bromide (entries 1–3). Both substrates gave the branched compound as the major product, but the proportion of the latter was significantly lower than that obtained with PhMgBr. As anticipated because of its greater encumbrance, the use of *o*-methylphenylmagnesium chloride resulted in a very low conversion (2% conversion after 1 h reaction time) although the branched product formed selectively (entry 4).

Table 3. Copper-catalysed allylic alkylation of cinnamyl bromide with arylmagnesium halide.[a]

Entry	ArMgX	NHC·HX	Conversion [%][b]	Branched [%][b]	Linear [%][b]
1	PhMgBr	**4**	100	78	22
2	*p*-Cl-(C$_6$H$_4$)MgBr	**4**	94	52	48
3	*p*-F-(C$_6$H$_4$)MgBr	**4**	100	62	38
4	*o*-Me-(C$_6$H$_4$)MgCl	**4**	2	100	0

[a] Reaction conditions: [Cu(OTf)$_2$] (1 mol-%), salt **4** (1 mol-%), PhCH=CHCH$_2$Br (0.32 mmol), ArMgX (0.39 mmol), Et$_2$O (3 mL), –78 °C, 1 h. [b] The conversion and the linear/branched proportions were determined by ^{1}H NMR spectroscopic analysis (accuracy of ± 5%).

In the generally accepted mechanism for copper-catalysed allylic substitutions (Scheme 5), the initially formed arylcuprate **A** preferentially reacts with the allylic bromide to form the σ-allyl copper(III) complex **B**. Reductive elimination of **B** leads to the branched product, whereas its isomerisation into the π-allyl complex **C** gives the sterically less hindered σ-allyl complex **D**, precursor of the linear product. Thus, the regioselectivity depends on the relative rates of the reductive elimination of **B**, the isomerisation of **B** to **D**, and the subsequent reductive elimination.[4,6,20–28] In these two possible pathways, a bulky ligand should accelerate the reductive elimination step leading to the γ-product. This was indeed observed with the ligands **1**–**4** (in this order) in the reaction between cinnamyl bromide and PhMgBr. In the same vein, the reductive elimination step leading to the γ-product should also be favoured with bulky Grignard reagents. This was notably the case with *o*-Me-C$_6$H$_4$MgCl. Thus, the present results conform to the generally accepted mechanism. The fact that the γ-selectivity of the most bulky ligand used in this study, namely the carbene derived from **4**, does not reach that of Tomioka's crowded complex **9**[9,10] (Figure 4), reflects the seemingly moderate steric encumbrance of **4** (electronic factors are not relevant here because the electronic influence of a mesityl group compares with that of an alkyl group[29]). We note, however, that the rate of arylation with the [Cu(OTf)$_2$]/**4** system (100% conversion in 1 h using 1 mol-% of copper catalyst) is comparable to that of **9**. Overall, the unexpectedly small influence of the bulky TPR group on the γ selectivity of the reaction contrasts with the previously reported major activity increase induced by this group in Suzuki–Miyaura cross coupling. Possibly, the steric influence on the selectivity of the TPR group in copper-catalysed allylic substitution could be en-



Scheme 5. Possible pathway for the copper-catalysed allylic substitution of cinnamyl bromide with arylmagnesium halides (ArMgX).

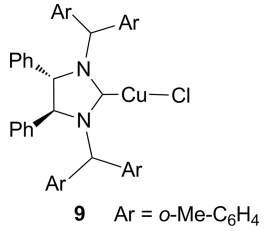


Figure 4. Tomioka's catalyst used in the arylation of cinnamyl bromide.

hanced by rigidly fixing the TPR unit (after chemical modification of the ligand) above the cavity entrance, thereby increasing its time-averaged steric bulk.

Conclusions

We have shown that the mono-TPR-substituted imidazolium salts used in this study efficiently catalyse the copper-catalysed arylation of cinnamyl bromide with phenylmagnesium bromide. The intrinsic ability of the bulky TPR group to induce γ-selectivity was found to be moderate, but formation of the branched product could be significantly increased by attaching appropriate substituents to the second nitrogen atom, with the highest b/l ratio being obtained for the imidazolium salts combining TPR and mesityl substituents. A rational way to improve the γ-selectivity with TPR substituted NHCs could involve restricting the rotational freedom of the carbene ring about the N–C(resorcinarenyl) moiety so as to force the metal centre to remain located permanently above the cavity entrance, and consequently render the steric effects of the TPR group predominant over those of the N2-substituent. This could then also promote possible cavity effects associated with the receptor properties of the resorcinarene unit. Modification of the electronic properties of such ligands could also be envisaged.

Experimental Section

General Experimental Methods: All manipulations were performed in Schlenk-type flasks under dry nitrogen. Solvents were dried by conventional methods and distilled immediately prior to use. $CDCl_3$ was passed down a 5 cm thick alumina column and stored under nitrogen over molecular sieves (4 Å). Routine ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with Bruker FT instruments (AVANCE 400). ^1H NMR spectra were referenced to residual protiated solvents (δ = 7.26 ppm for $CDCl_3$) and ^{13}C NMR chemical shifts are reported relative to deuteriated solvents (δ = 77.16 ppm for $CDCl_3$). Chemical shifts and coupling constants are reported in ppm and in Hz, respectively. Elemental analyses were performed by the Service de Microanalyse, Institut de Chimie, Université de Strasbourg. 2-*N*-Benzyl-5-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-yl]imidazolinium bromide (**1**),[13] 2-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-methyl]-5-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-yl]imidazolinium bromide (**2**),[12] 5-*N*-imidazolyl-4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene (**5**),[13] 2-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-methyl]-5-*N*-[25,26,27,28-tetrabenzyloxycalix[4]arene-5-yl]imidazolinium bromide (**8**),[12] and 2,6-dimethoxybenzyl bromide[30] were prepared according to reported procedures.

General Procedure for the Preparation of the Imidazolium Salts 3 and 7: *N*-Arylimidazole (0.25 mmol) and alkyl bromide (0.25 mmol) were dissolved in $CHCl_3$ (10 mL). The reaction mixture was then heated to reflux for 2 d. After cooling to room temperature, the solvent was removed under vacuum. The solid was washed with pentane and recrystallised from CH_2Cl_2/isopropyl ether to afford the corresponding imidazolium salt.

2-*N*-(2,6-Dimethoxybenzyl)-5-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-yl]imidazolinium Bromide (3): Yield 0.249 g (90%). ^1H NMR (400 MHz, $CDCl_3$): δ = 9.85 (s, 1 H, NCHN), 7.34 [t, ^3J = 8.5 Hz, 1 H, ArH, $(CH_3O)_2C_6H_3$], 7.33 (s, 1 H, ArH, resorcinarene), 7.29 (br. s, 1 H, NC*H*CHN), 7.21 (br. s, 1 H, NCHC*H*N), 7.12 (s, 3 H, ArH, resorcinarene), 6.64 (s, 2 H, ArH, resorcinarene), 6.60 [d, ^3J = 8.5 Hz, 2 H, ArH, $(CH_3O)_2C_6H_3$], 6.53 (s, 1 H, ArH, resorcinarene), 5.77 (s, 2 H, NCH_2Ar), 5.72 and 4.65 (AB spin system, ^2J = 7.2 Hz, 4 H, OCH_2O), 5.60 and 4.77 (AB spin system, ^2J = 7.5 Hz, 4 H, OCH_2O), 4.75 (t, ^3J = 7.8 Hz, 2 H, C*H*CH_2), 4.70 (t, ^3J = 8.1 Hz, 2 H, C*H*CH_2), 3.89 (s, 6 H, OCH_3), 2.30–2.16 (m, 8 H, CHCH_2), 1.49–1.29 (m, 24 H, CH_2CH_2CH_2CH$_3$), 0.91 (t, ^3J = 6.9 Hz, 12 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.92–104.23 (ArC), 137.56 (s, NCN), 122.90 (s, N*C*HCHN), 117.79 (s, NCH*C*HN), 101.17 (s, OCH_2O), 99.57 (s, OCH_2O), 56.30 (s, OCH_3), 43.12 (s, NCH_2Ar), 36.80 (s, *C*HCH$_2$), 36.49 (s, *C*HCH$_2$), 32.17 (s, *C*H$_2$CH$_2$CH$_3$), 32.05 (s, *C*H$_2$CH$_2$CH$_3$), 30.12 (s, CH*C*H$_2$), 29.90 (s, CH*C*H$_2$), 27.70 (s, CHCH$_2$*C*H$_2$), 27.65 (s, CHCH$_2$*C*H$_2$), 22.82 (s, *C*H$_2$CH$_3$), 22.79 (s, *C*H$_2$CH$_3$), 14.24 (s, CH$_2$*C*H$_3$), 14.22 (s, CH_2CH_3) ppm. MS (ESI-TOF): *m*/*z* = 1033.54 $[M - Br]^+$ (expected isotopic profile). $C_{64}H_{77}BrN_2O_{10}$ (1114.21): calcd. C 68.99, H 6.97, N 2.51; found C 69.12, H 7.17, N 2.39.

2-*N*-[4(24),6(10),12(16),18(22)-Tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-methyl]-5-*N*-phenyl-imidazolinium Bromide (7): Yield 0.249 g (95%). ^1H NMR (400 MHz, $CDCl_3$): δ = 10.86 (s, 1 H, NCHN), 7.69 (d, ^3J = 7.2 Hz, 2 H, ArH, Ph), 7.60–7.51 (m, 3 H, ArH, Ph), 7.47 (br. s, 1 H, NC*H*CHN), 7.36 (br. s, 1 H, NCHC*H*N), 7.21 (s, 1 H, ArH, resorcinarene), 7.09 (s, 1 H, ArH, resorcinarene), 7.08 (s, 2 H, ArH, resorcinarene), 6.55 (s, 2 H, ArH, resorcinarene), 6.48 (s, 1 H, ArH, resorcinarene), 6.17 and 4.55 (AB spin system, ^2J = 7.4 Hz, 4 H, OCH_2O), 5.80 (s, 2 H, NCH_2), 5.64 and 4.45 (AB spin system, ^2J = 7.2 Hz, 4 H, OCH_2O), 4.72 (t, ^3J = 8.2 Hz, 2 H, C*H*CH_2), 4.70 (t, ^3J = 8.2 Hz, 2 H, C*H*CH_2), 2.33–2.08 (m, 8 H, CHCH_2), 1.43–1.29 (m, 24 H, CH_2CH_2CH_2CH$_3$), 0.90 (t, ^3J = 7.2 Hz, 6 H, CH_2CH_3), 0.90 (t, ^3J = 7.2 Hz, 6 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.37–116.81 (ArC), 134.56 (s, NCN), 122.05 (s, N*C*HCHN), 119.88 (s, NCH*C*HN), 100.53 (s, OCH_2O), 99.68 (s, OCH_2O), 44.23 (s, NCH_2), 36.76 (s, *C*HCH$_2$), 36.45 (s, *C*HCH$_2$), 32.14 (s, *C*H$_2$CH$_2$CH$_3$), 32.11 (s, *C*H$_2$CH$_2$CH$_3$), 30.02 (s, CH*C*H$_2$), 29.92 (s, CH*C*H$_2$), 27.67 (s, CHCH$_2$*C*H$_2$), 22.80 (s, *C*H$_2$CH$_3$), 22.78 (s, *C*H$_2$CH$_3$), 14.21 (s, CH$_2$*C*H$_3$) ppm. MS (ESI-TOF): *m*/*z* = 973.53 $[M - Br]^+$ (expected isotopic profiles). $C_{62}H_{73}BrN_2O_8$ (1054.16): calcd. C 70.64, H 6.98, N 2.55; found C 70.49, H 7.02, N 2.64.

2-*N*-[2,4,6-Trimethylphenyl]-5-*N*-[4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]arene-5-yl]imidazolinium Triflate (4): A mixture of *N*-resorcinarenyl-imidazole **5** (0.500 g, 0.57 mmol), dimesitylidonium salt (0.437 g, 0.85 mmol) and $[Cu(OTf)_2]$ (0.010 g, 0.03 mmol, 5 mol-%) in DMF (3 mL) was stirred at 100 °C for 16 h. The solvent was then removed under reduced pressure and the solid residue was purified by flash chromatography (acetone/MeOEt, 10:90 v/v), yield 0.309 g (48%). ^1H NMR (500 MHz, $CDCl_3$): δ = 9.1 (s, 1 H, NCHN), 7.55 (br. s, 1 H, NC*H*CHN), 7.41 (s, 1 H, ArH, resorcinarene), 7.36 (s br, 1 H, NCHC*H*N), 7.15 (s, 2 H, ArH, resorcinarene), 7.13 (s, 1 H, ArH, resorcinarene), 7.03 (s, 2 H, ArH, mesityl), 6.53 (s, 2 H, ArH, resorcinarene), 6.46 (s, 1 H, ArH, resorcinarene), 5.66 and 4.47 (AB spin system, ^2J = 7.5 Hz, 4 H, OCH_2O), 5.53 and 4.68 (AB spin system, ^2J = 7.5 Hz, 4 H, OCH_2O), 4.73 (t, ^3J = 8.0 Hz, 2 H, C*H*CH_2), 4.73 (t, ^3J = 8.0 Hz, 2 H, C*H*CH_2), 2.34 (s, 3 H, *p*-CH_3-mesityl), 2.32–2.07 (m, 8 H, CHCH_2), 2.07 (s, 6 H, *o*-CH_3-mesityl), 1.46–1.32 (m, 24 H, CH_2CH_2CH_2CH$_3$), 0.92 (t, ^3J = 7.5 Hz, 6 H,

CH_2CH_3), 0.91 (t, ^3J = 7.5 Hz, 6 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.56–117.19 (ArC), 100.55 (s, OCH_2O), 99.50 (s, OCH_2O), 36.81 (s, *C*HCH$_2$), 36.46 (s, *C*HCH$_2$), 32.16 (s, *C*H$_2$CH$_2$CH$_3$), 32.04 (s, *C*H$_2$CH$_2$CH$_3$), 30.09 (s, CH*C*H$_2$), 29.91 (s, CH*C*H$_2$), 27.69 (s, CHCH$_2$*C*H$_2$), 27.66 (s, CHCH$_2$*C*H$_2$), 22.79 (s, *C*H$_2$CH$_3$), 22.78 (s, *C*H$_2$CH$_3$), 21.24 (s, *p*-CH$_3$-mesityl), 17.18 (s, *o*-CH$_3$-mesityl), 14.20 (s, CH$_2$*C*H$_3$) ppm. MS (ESI-TOF): *m*/*z* = 1001.58 [M – TfO]$^+$ (expected isotopic profiles). $C_{65}H_{77}F_3N_2O_{11}S$ (1151.37): calcd. C 67.81, H 6.74, N 2.43; found C 67.77, H 6.82, N 2.79.

Bromo-[2-{4(24),6(10),12(16),18(22)-tetramethylenedioxy-2,8,14,20-tetrapentylresorcin[4]aren-5-yl}-5-benzylimidazol-2-ylidene]copper(I) (6): A mixture of [CuBr] (0.041 g, 0.28 mmol), imidazolium salt **1** (0.300 g, 0.28 mmol) and NaO*t*Bu (0.027 g, 0.28 mmol) in THF (5.5 mL) was stirred at room temp. for 4 h. The reaction mixture was then filtered through Celite. The filtrate was evaporated under vacuum, and the solid residue purified by flash chromatography (MeOH/CH_2Cl_2, 5:95 v/v) to afford the corresponding white copper complex **6**, yield 0.120 g (38%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 3 H, ArH, Ph), 7.33 (br. s, 1 H, NC*H*NCH), 7.18 (d, ^3J = 6.5 Hz, 2 H, ArH, Ph), 7.15 (s, 2 H, ArH, resorcinarene), 7.14 (br. s, 1 H, NCHNC*H*), 6.98 (s, 1 H, ArH, resorcinarene), 6.94 (s, 1 H, ArH, resorcinarene), 6.53 (s, 3 H, ArH, resorcinarene), 5.71 and 4.55 (AB spin system, ^2J = 7.0 Hz, 4 H, OCH_2O), 5.36 and 4.78 (AB spin system, ^2J = 7.0 Hz, 4 H, OCH_2O), 5.30 (s, 2 H, NCH_2Ph), 4.73 (t, ^3J = 8.0 Hz, 4 H, C*H*CH$_2$), 2.31–2.21 (m, 8 H, CHC*H*$_2$), 1.46–1.33 (m, 24 H, C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.93 (t, ^3J = 7.0 Hz, 6 H, CH_2CH_3), 0.92 (t, ^3J = 7.0 Hz, 6 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.76–117.00 (ArC), 135.56 (s, NCN), 126.52 (s, N*C*HCHN), 124.50 (s, NCH*C*HN), 100.15 (s, OCH_2O), 100.09 (s, OCH_2O), 55.31 (NCH_2Ph), 36.80 (s, *C*HCH$_2$), 36.52 (s, *C*HCH$_2$), 32.23 (s, *C*H$_2$CH$_2$CH$_3$), 32.15 (s, *C*H$_2$CH$_2$CH$_3$), 30.20 (s, CH*C*H$_2$), 29.89 (s, CH*C*H$_2$), 27.76 (s, CHCH$_2$*C*H$_2$), 22.86 (s, *C*H$_2$CH$_3$), 14.27 (s, CH$_2$*C*H$_3$) ppm. MS (ESI-TOF): *m*/*z* = 1076.48 [M – Br + CH_3CN]$^+$ (expected isotopic profile). $C_{62}H_{72}BrCuN_2O_8$·*i*Pr$_2$O (1116.69 + 60.09): calcd. C 66.34, H 6.85, N 2.38; found C 66.42, H 6.91, N 2.18. The sample used for elemental analysis was obtained by recrystallisation of **6** from a CH_2Cl_2/*i*Pr$_2$O solution.

X-ray Analysis of 6: Single crystals of **6**·1.5Et$_2$O suitable for an X-ray diffraction study were obtained by slow diffusion of diethyl ether into an acetonitrile solution of the complex. M_r = 1222.81; triclinic; space group $P\bar{1}$; a = 14.2710(4), b = 17.1546(5), c = 17.4082(4) Å, α = 115.880(3), β = 94.672(2), γ = 109.233(3)°; V = 3490.76(22) Å^3; Z = 2; D_x = 1.163 mg m^{-3}; λ(Mo-K_α) = 0.71073 Å; μ = 0.937 mm^{-1}; F(000) = 1288; T = 220(2) K. The sample (0.45 × 0.41 × 0.27 mm) was studied with an Oxford Diffraction Xcalibur Sapphire 3 diffractometer (graphite-monochromated Mo-K_α radiation, λ = 0.71073 Å). The data collection ($2\theta_{max}$ = 27°, omega scan frames via 0.7° omega rotation and 30 s per frame, range *HKL*: *H* –18, 18 *K* –21, 21 *L* –22,22) gave 15029 reflections. The data led to 8705 independent reflections with $I > 2.0\sigma(I)$. The structure was solved with SIR-97,[31] which revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, all the hydrogen atoms were found from the Fourier difference map. The whole structure was refined with SHELX97[32] by full-matrix least-squares techniques (use of $|F^2|$; *x*, *y*, *z*, β_{ij} for C, Br, Cu, N and O atoms, *x*, *y*, *z* in riding mode for H atoms); 736 variables and 8705 observations with $I > 2.0\sigma(I)$; calcd. $w = 1/[\sigma^2(F_o^2) + (0.1128P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting R = 0.0539, R_W = 0.1814 and S_W = 1.023, $\Delta\rho < 1.19$ e Å^{-3}. The major issues in the structure determination arose from the tendency of the crystal to de-solvate rapidly and a phase transition, which occurs around 200 K and led to decomposition of the sample. The checkcif contains two level A alerts, both due to the disordered diethyl ether lying outside the cavity. Given that it was not possible to assign the corresponding residuals peaks, the SQUEEZE procedure was applied.

Crystallographic data CCDC-844297 for compound **6** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Typical Procedure for the Copper-Catalysed Allylic Arylations at –78 °C: A 15 mL Schlenk tube was filled with [Cu(OTf)$_2$] (1.2 mg, 1 mol-%), ligand (1 mol-%) and Et$_2$O (2 mL). The reaction mixture was stirred for 10 min at 0 °C before addition of the Grignard reagent (0.39 mmol). After cooling the reaction mixture to –78 °C, a solution of cinnamyl bromide (64 mg, 0.32 mmol) in Et$_2$O (1 mL) was added quickly. After 1 h (the temperature being maintained at –78 °C), 1 M aq HCl (1 mL) was added. After extraction of the aqueous layer with Et$_2$O (2 × 2 mL), the organic phases were combined. The resulting solution was washed with $NaHCO_3$ (5 mL), brine (5 mL), dried with $MgSO_4$, filtered and evaporated under reduced pressure. The product distribution was analysed by ^1H NMR spectroscopy.

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[1] *Copper-Mediated Cross-Coupling Reactions* (Eds.: G. Evano, N. Blanchard), John Wiley & Sons, Hoboken, New Jersey, USA, **2014**.
[2] S. Díez-González, S. P. Nolan, *Synlett* **2007**, 2158–2167.
[3] J.-B. Langlois, A. Alexakis, *Top. Organomet. Chem.* **2012**, *38*, 235–268.
[4] J.-E. Bäckvall, M. Sellén, B. Grant, *J. Am. Chem. Soc.* **1990**, *112*, 6615–6621.
[5] G. Fouquet, M. Schlosser, *Angew. Chem. Int. Ed. Engl.* **1974**, ***13***.
[6] S. Ando, H. Matsunaga, T. Ishizuka, *Tetrahedron* **2013**, *69*, 1687–1693.
[7] D. Grassi, H. Li, A. Alexakis, *Chem. Commun.* **2012**, *48*, 11404–11406.
[8] M. Magrez, Y. Le Guen, O. Baslé, C. Crévisy, M. Mauduit, *Chem. Eur. J.* **2013**, *19*, 1199–1203.
[9] K. B. Selim, Y. Matsumoto, K. Yamada, K. Tomioka, *Angew. Chem. Int. Ed.* **2009**, *48*, 8733–8735; *Angew. Chem.* **2009**, *121*, 8889.
[10] K. B. Selim, H. Nakanishi, Y. Matsumoto, Y. Yamamoto, K. Yamada, K. Tomioka, *J. Org. Chem.* **2011**, *76*, 1398–1408.
[11] S. Tominaga, Y. Oi, T. Kato, D. K. An, S. Okamoto, *Tetrahedron Lett.* **2004**, *45*, 5585–5588.
[12] N. Şahin, D. Sémeril, E. Brenner, D. Matt, I. Özdemir, C. Kaya, L. Toupet, *Turk. J. Chem.*, DOI: 10.3906/kim-1503–82.
[13] N. Şahin, D. Sémeril, E. Brenner, D. Matt, I. Özdemir, C. Kaya, L. Toupet, *ChemCatChem* **2013**, *5*, 1115–1125.
[14] N. Şahin, D. Sémeril, E. Brenner, D. Matt, I. Özdemir, C. Kaya, L. Toupet, *Eur. J. Org. Chem.* **2013**, 4443–4449.
[15] The relatively low isolated yield arises from the fact that separation of this complex from unreacted imidazolium salt was difficult.
[16] H. El Moll, D. Sémeril, D. Matt, L. Toupet, *Eur. J. Org. Chem.* **2010**, 1158–1168.

[17] H. El Moll, D. Sémeril, D. Matt, L. Toupet, J.-J. Harrowfield, *Org. Biomol. Chem.* **2012**, *10*, 372–382.
[18] H. El Moll, D. Sémeril, D. Matt, M.-T. Youinou, L. Toupet, *Org. Biomol. Chem.* **2009**, *7*, 495–501.
[19] The degree of steric encumbrance of the carbene ligands derived from **1**–**4** is difficult to quantify accurately because it depends on the position of the metal with respect to the cavity. The proposed order of increasing bulk (**1** < **2** < **3** < **4**) presumes that the metal is pushed away from the cavity, as shown in Figure 2, and that the N2 substituent is oriented so as to come as close as possible to the coordinated metal centre.
[20] J.-E. Bäckvall, E. S. M. Persson, A. Bombrun, *J. Org. Chem.* **1994**, *59*, 4126–4130.
[21] E. J. Corey, N. W. Boaz, *Tetrahedron Lett.* **1984**, *25*, 3063–3066.
[22] H. L. Goering, S. S. Kantner, *J. Org. Chem.* **1984**, *49*, 422–426.
[23] H. L. Goering, V. D. J. Singleton, *J. Am. Chem. Soc.* **1976**, *136*, 7854–7855.
[24] H. L. Goering, V. D. J. Singleton, *J. Org. Chem.* **1983**, *48*, 1531–1533.
[25] J. Levisalles, M. Rudler-Chauvin, H. Rudler, *J. Organomet. Chem.* **1977**, *136*, 103–110.
[26] R. M. Magid, *Tetrahedron* **1980**, *36*, 1901–1930.
[27] E. S. M. Persson, M. van Klaveren, D. M. Grove, J.-E. Bäckvall, G. van Koten, *Chem. Eur. J.* **1995**, *1*, 351–359.
[28] T. L. Underiner, H. L. Goering, *J. Org. Chem.* **1991**, *56*, 2563–2672.
[29] R. A. Kelly III, H. Clavier, S. Giudice, N. M. Scott, E. D. Stevens, J. Bordner, I. Samardjiev, C. D. Hoff, L. Cavallo, S. P. Nolan, *Organometallics* **2008**, *27*, 202–210.
[30] L. Feng, K. Lv, M. Liu, S. Wang, J. Zhao, X. You, S. Li, J. Cao, H. Guo, *Eur. J. Med. Chem.* **2012**, *55*, 125–136.
[31] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Crystallogr.* **1998**, *31*, 74–77.
[32] G. M. Sheldrick, *SHELXL-97*, *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, **1997**.
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