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Synthesis of Extended Chromogenic Tetra-(p-substituted-phenyl)-tetraethoxycalix[4]arenes

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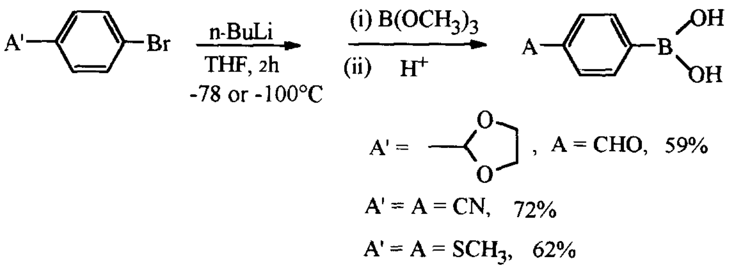
Abstract: Synthesis of cone conformer of donor-acceptor phenylcalix[4]arene derivatives was achieved by palladium(0) catalysed cross coupling reactions.

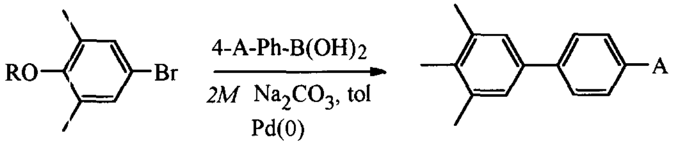
Calixarenes, attractive preorganized building blocks for artifical receptors, have been widely studied for inorganic cation complexation.[1] On the other hand, attention has been already drawn on hosting of polar or non-polar organic molecules which requires a relatively deep cavity to bind larger organic guests.[2] Furthermore, the use of chromogenic calixarenes for the applications of optical sensors[3] and second-order nonlinear optical materials[4] has recently aroused much interest. Consequently, the development of versatile synthetic methods for the preparation of new classes of extended chromogenic calixarenes may be of interest.

We explored the Suzuki's type crossing coupling reaction,[5] catalysed by various palladium(0) complexes to synthesize extended calix[4]arene derivatives **1a**, **1b** and **1d** bearing with donors and acceptors. The p-substituted phenylboronic acids were prepared by lithium-halogen exchange of the corresponding bromobenzene derivatives at low temperature and followed by treatment with the trimethylborate. After hydrolysis, the desired arylboronic acids were obtained in good yields, as summarized in scheme 1. This method was found to be convenient and efficient for the preparation of arylboronic acids.



Scheme 1

The use of catalytic amount of different palladium complexes including tetrakis(triphenylphosphine)palladium(0) and bis(tris-o-tolylphosphine)palladium(0),[6] generated *in situ* from palladium acetate and tris-o-tolylphosphine, was initially carried out to prepare 4,4'-donor-acceptor biphenyl derivatives **3a-e** before pursuing the synthesis of functionalized calixarenes. The reaction conditions and results were presented in Table 1. Both of the complexes catalysed the coupling reaction efficiently and afforded comparable yields. In general, the use of tris-o-tolylphosphine palladium complex as catalyst offers milder reaction conditions; however, in the preparation of **3d**, methyl ethoxybiphenylcarboxylate was isolated as the side product.



3a: $R = CH_3$, $A = CHO$
3b: $R = CH_3$, $A = CN$
3c: $R = CH_3$, $A = SCH_3$
3d: $R = C_2H_5$, $A = CHO$
3e: $R = C_2H_5$, $A = CN$

Table 1. Cross Coupling Reactions of 4-Bromo-2,6-dimethylphenyl alkyl ethers with Arylboronic acids

Compounds	Catalysts	Temperature (°C)	Time (h)	Isolated yield (%)
3a	5 mole% $Pd(Ph_3)_4$	80-85	12	54
3b	5 mole% $Pd(Ph_3)_4$	80-85	12	70
3c	5 mole% $Pd(Ph_3)_4$	80-85	12	90
3d	5 mole% $Pd(OAc)_2$:2P(o-tol)$_3$	70-75	3	52[a]
3e	5 mole% $Pd(OAc)_2$:2P(o-tol)$_3$	70-75	3	96

[a] 4% of methyl ethoxybiphenylcarboxylate was isolated

To stabilize the cone conformation of the chromogenic calix[4]arene derivatives, in which all the chromophores are essentially oriented in the same direction, ethyl substituents on the phenolic oxygens were introduced using the conditions described by Reinhoudt *et al.* [7] Bromination[8] of calix[4]arene tetraethyl ether with NBS afforded precursor **2** in good yield (81%).

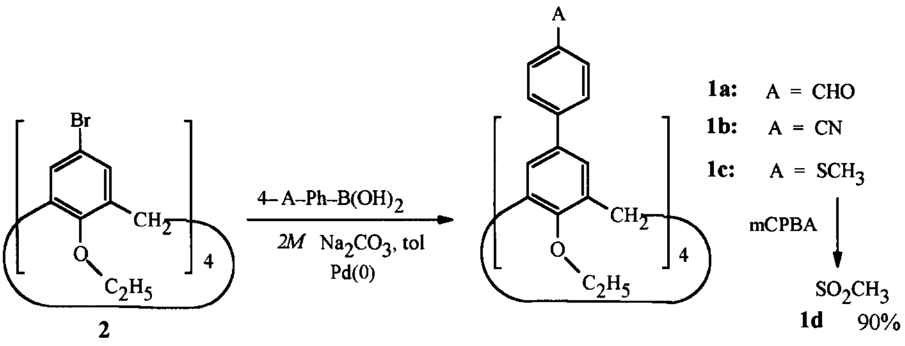


Table 2. Cross Coupling Reactions of **2** with Arylboronic acids

Compounds	Catalysts	Temperature (°C)	Time (h)	Isolated yield[b] (%)
1a	25 mole% $Pd(Ph_3)_4$	80-85	7[a]	15
1b	25 mole% $Pd(Ph_3)_4$	80-85	7[a]	37
1c	25 mole% $Pd(Ph_3)_4$	80-85	7[a]	42
1b	20 mole% $Pd(OAc)_2{:}2P(o\text{-}tol)_3$	70-75	3	61
1c	20 mole% $Pd(OAc)_2{:}2P(o\text{-}tol)_3$	70-75	3	72

[a] longer reaction time doesn't afford better yield. [b] only cone conformer was considered as desired product.

Since the framework of the calix[4]arene was composed of 4 chromogens, a 4-fold excess of the catalyst was used in order to keep the optimized reaction conditions.[9] The reaction conditions and results were summarized in Table 2. No attempt was made to use the tris-o-tolylphosphine palladium complex for the synthesis of **1a** because this catalyst caused a side reaction with the aldehyde functionality. Again, $Pd(OAc)_2{:}2P(o\text{-}tol)_3$ was found to be more efficient than $Pd(Ph_3)_4$ complex. An oxidation of **1c** by mCPBA gave **1d** in 90% yield.

In conclusion, we have successfully illustrated the use of palladium(0) catalysed cross coupling reactions to synthesize donor-acceptor phenylcalix[4]arene derivatives. The possible use of these chromogenic calix[4]arene derivatives for building new nonlinear optical materials is under current investigations.

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9. To a stirred solution of **2** (0.35 to 0.59 mmole) and 20 mole % of $Pd(OAc)_2$:2P(o-tol)$_3$ in 15 mL of toluene was added under N_2 5 mL of 2*M* Na_2CO_3 and 6 eqv. of arylboronic acid in 10 mL of methanol respectively. After being heated to 70-75 °C for 3h, the reaction mixture was added with 50 mL of 2*M* Na_2CO_3 containing 5 mL of conc. NH_3 and then extracted twice with CH_2Cl_2 (50 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated to dryness. The crude product was purified by silica-gel column chromography using CH_2Cl_2 as eluant. **1a**: mp 229-230 °C; ^1H NMR ($CDCl_3$, 20 °C and 200 MHz): δ 1.56 (t, 3, J = 7 Hz, CH_3), 3.35 (d, 1, J = 13.4 Hz, $ArCH_2Ar$), 4.55 (q, 2, J = 6 Hz, OCH_2), 4.61 (d, 1, J = 13.2 Hz, $ArCH_2Ar$), 7.01 (s, 2, calixarene H), 7.25 (d, 2, J = 8.0 Hz, ArH), 7.59 (d, 2, J = 8.2 Hz, ArH), 9.87 (s, 1, CHO); ^{13}C NMR ($CDCl_3$, 20 °C and 50.3 MHz): δ 191.7, 156.9, 146.7, 135.8, 134.4, 133.6, 129.9, 127.1, 126.7, 70.6, 31.3, 15.7. **1b**: mp 234-235 °C; ^1H NMR ($CDCl_3$, 20 °C and 200 MHz): δ 1.53 (t, 3, J = 7.3 Hz, CH_3) 3.31 (d, 1, J = 13.4 Hz, $ArCH_2Ar$), 4.12 (q, 2, J = 7 Hz, OCH_2), 4.59 (d, 1, J = 13.4 Hz, $ArCH_2Ar$), 6.93 (s, 2, calixarene H), 7.18 (d, 2, J = 8.4 Hz, ArH) 7.42 (d, 2, J = 8.2 Hz, ArH); ^{13}C NMR ($CDCl_3$, 20° C and 50.3 MHz): δ 157.0, 145.0, 135.8, 133.0, 132.1, 126.9, 126.8, 118.7, 110.0, 70.6, 31.3, 15.6. **1d**: mp 206-207 °C. ^1H NMR ($CDCl_3$, 20 °C and 200 MHz): δ 1.58 (t, 3, J = 6.9 Hz, CH_3), 3.10 (s, 3, SO_2CH_3), 3.35 (d, 1, J = 13 Hz, $ArCH_2Ar$), 4.15 (q, 2, J = 7 Hz, OCH_2), 4.62 (d, 1, J = 13 Hz, $ArCH_2Ar$), 7.00 (s, 2, calixarene H), 7.37 (d, 2, J = 8.4 Hz, ArH), 7.79 (d, 2, J = 8.4 Hz, ArH); ^{13}C NMR ($CDCl_3$, 20 °C and 50.3 MHz): δ 158.9, 146.4, 135.8, 135.7, 133.3, 127.6, 127.3, 127.2, 70.7, 44.4, 31.4, 15.8.

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