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Superacid BF_3-H_2O promoted benzylation of arenes with benzyl alcohols and acetates initiated by the trace of water

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A convenient procedure employing simple starting materials benzyl alcohols and acetates as the benzyl donor to assemble a series of diarylalkanes through benzylation of arenes using *in situ* prepared superacid BF_3-H_2O as an efficient promotor has been developed. The beneficial role of water to the reaction has been clarified with combination of control experiments and ^{11}B NMR analysis. This reaction is a self-promoted model, which is triggered by the trace of water and continuously promoted by self released by-product water (or carboxylic acid). A wide range of substrates are investigated and the moderate to excellent yields and the good regioselectivities for secondary benzyl alcohols as well as arenes bearing electron-withdrawing groups have been achieved. As a result, moisture in reaction system has been eventually utilized as an efficient initiator in all benzylation cases.

Introduction

Diarylalkane fragments act as pharmacologically activecompounds such as piritrexim, trimethoprim and avrainvilleol as well as key subunits of functional materials such as calixarene, cryptophane and pillar[n]arene (Figure 1).[1] In addition, they can be used in the preparation of electroactive and photoactive oligomers and polymers.[2] In the past years, the methods of synthesizing diarylalkanes have been reported by reductions of diarylketones or diarylcarbinols.[3] Moreover, some transition-metal-catalyzed cross-coupling strategies for the generation of diarylalkanes have been developed, involving Pd,[4] Fe,[5] Ir[6] and Ni[7]. As an alternative protocol, the Friedel-Crafts reaction of benzylic halides with arenes is considered to be one of the most powerful tools for the synthesis of diarylalkane derivatives.[8-10] In addition to benzyl halides, benzyl alcohols, acetates, carbonates, silyl esters, alkyl esters and benzyl hydroxamates have been successfully introduced to meet the requirements of green chemistry by cleaving heterolytically the C-O bond to construct C-C bond in preparation of diarylalkanes.[11-22] The substitution of activated alcohols is frequently used in organic chemistry and this transformation has been encouraged and listed as one of key green chemistry research priority areas in the American Chemical Society (ACS) Green Chemistry Institute (GCI) roundtable. Considering the pursuit of green chemistry for a sustainable business and environment, benzyl alcohols and acetates are more preferable in low cost and commercial availability, and by-products released after reaction are only environmentally benign water or acetic acid.[23]

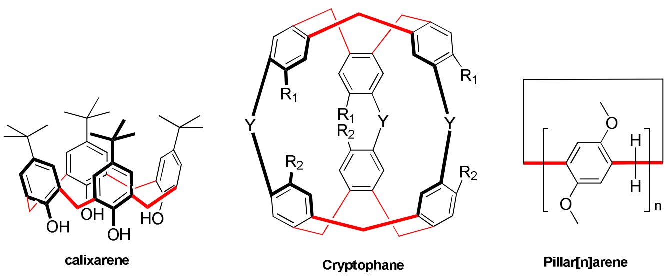


Figure 1. Examples of diarylalkanes in supramolecules.

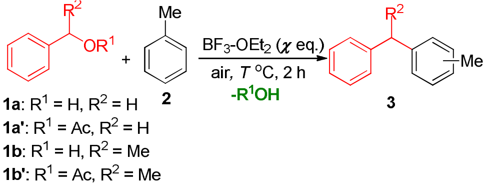
BF_3-OEt_2 (or BF_3) is usually utilized as a Lewis acid due to its empty *p*-orbital, and has shown strong interaction with numerous ligands due to the boron atom acting as an acceptor to form a large number of coordinate compounds containing carbon, nitrogen, oxygen, fluorine, phosphorus and sulfur.[24] For instance, BF_3-OEt_2 is an adduct of BF_3 and Et_2O through a donor-acceptor bonding.[25] Various synthetic procedures such as alkylation,[22,26a] cyclization,[26b,e] rearrangement[26c] and coupling reactions[26d] employing BF_3-OEt_2 have been reported. In the opposite way, the superacid boron trifluoride monohydrate (BF_3-H_2O) formed by mixing BF_3 and water in equal amount has served as a highly effective acid catalyst for several Friedel-Craft reactions and become a very extensively studied area.[27] Compared to Et_2O, the interaction of H_2O with BF_3 is stronger, and ligand exchange has been observed between BF_3-OEt_2 and water to form superacid BF_3-H_2O.[28]

Direct nucleophilic substitution of an alcohol through OH activation is attractive as it yields water as the by-product, however hydroxide is a poor leaving group usually requiring activation. Based on an early report, BF_3 gas has been utilized to promote the Friedel-Crafts alkylation of benzene with alcohols under open-flask conditions in up to gram scale, in which mono-/di-/polybenzylbezenes were obtained in yields of 23%, 15% and 34%, respectively.[29] To the best of our knowledge, the true role of BF_3 in this reaction has not been clarified and the substrate generality has not been investigated to date. Recently we have reported benzylation of arenes with benzyl ethers and illustrated the crucial role of moisture throughout the paper.[30] Herein we are delighted to report an efficient self-promoted monobenzylation of arenes to assembly the structurally diverse diarylmethanes with benzyl alcohols and acetates triggered by the trace of water. The beneficial role of water has been investigated in detail, not the BF_3-OEt_2 but the *in situ* generated superacid BF_3-H_2O has proved to be the actual promoter in this transformation and the merit that the superacid BF_3-H_2O is formed with mainly by-product water has enhanced its synthetic appeal.

Results and discussion

In our initial study, we chose the reaction of simple benzyl alcohol (**1a**) with toluene (**2**) as a starting point for our investigation. The treatment of benzyl alcohol (**1a**) with 20 mol% BF_3-OEt_2 only yielded a trace amount of desired product **3** (Table 1, entry 1). Increasing the amount of BF_3-OEt_2 to 1.0 equivalent resulted in a significant increase in yield giving 82% of **3** as a mixture of isomers (Table 1, entry 2). 1.2 Equivalents resulted in an increased yield of 89% and a similar ratio of isomers (Table 1, entry 3). Increasing the amount of BF_3-OEt_2 beyond 1.2 equivalents had a similar level on either the yield or the ratio of observed products **3** (Table 1, entries 4-6). Increasing reaction temperature to reflux proved to be less favorable as the yields were slightly lower compared to reactions run at 80 °C (Table 1, entry 7). In agreement with the report by Schäfer and Bode, we observed only 6% NMR-yield of the desired product when running the reaction at 25 °C (Table 1, entry 8). In an attempt to reduce the amount of arene, we tested $CHCl_3$ as a solvent which resulted in a diminished, yet a promising yield of 58% (Table 1, entry 9). By using 2.0 equivalents of BF_3-OEt_2, we could also use benzyl acetate (**1a'**), 1-phenyl ethanol (**1b**) and 1-phenyl ethylacetate (**1b'**) (Table 1, entries 10-12). The yields were excellent for all three benzyl donors. As expected the regioselectivities were significantly better favoring the *para*-product **3** when using sterically more encumbered **1b** and **1b'**.

Table 1. Optimization of Reaction Conditions.[a]

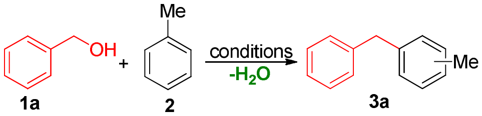


Entry	1	χ	T(°C)	Yield (%)[b], ratio (*o*- : *p*- : *m*-)[c]
1	**1a**	0.2	80	3 (-)
2	**1a**	1.0	80	82 (42:52:6)
3	**1a**	1.2	80	89 (42:53:5)
4	**1a**	1.5	80	91 (44:50:6)
5	**1a**	2.0	80	96 (41:53:6)
6	**1a**	2.5	80	93 (41:53:6)
7	**1a**	1.2	reflux	81 (41:52:7)
8[d]	**1a**	1.2	25	6 (-)
9[e]	**1a**	1.2	80	58 (44:49:7)
10	**1a'**	2.0	80	86 (42:51:7)
11	**1b**	2.0	80	91 (5:90:5)
12[f]	**1b'**	2.0	80	89 (12:88)

[a] Conditions: benzylic alcohols or acetates (**1**; 1.0 mmol), undistilled toluene (**2**; 2.0 mL), BF_3-OEt_2 (specified), temperature (specified), 2 h in air. [b] Yields of isolated products. [c] Isomer ratios determined by ^{13}C NMR. [d] Yield determined by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard. [e] Toluene (**2**, 0.5 mL, 4.6 mmol), $CHCl_3$ (1.5 mL). [f] No *m*-isomer was detected.

^{11}B NMR analysis was employed and the chemical shifts of the following signal peaks of H_3BO_3, BF_3-OEt_2, BF_3-$2H_2O$ and HBF_4-OEt_2, were observed at 19.49 ppm, -0.04 ppm, -1.6 ppm and -3.50 ppm, respectively.[31] When 1.0 equivalent of H_2O was added into BF_3-OEt_2, the signal was firstly broadened and eventually shifted to -0.94 ppm, which suggested an exchange process (admittedly a slow process) and formation of superacid BF_3-H_2O occurs. Moreover, hydration experiments of BF_3-OEt_2 did not lead to HBF_4 and H_3BO_3. Using Bode's reaction conditions, benzylations with benzyl alcohol and acetate resulted in low activities (=/<5% yield).[17c] It should be noted that these experiments were carried out under an atmosphere of dry N_2. We adapted the optimal conditions to the use of free benzyl alcohol and toluene (Table 1, entry 3), BF_3-OEt_2 was insoluble in toluene and two phases were observed before and after the reaction. At 80 °C the benzylation, carried out under an atmosphere of dry N_2, only led to a yield of 31% with the regioselectivity of 44:48:8 (*o*-: *p*-: *m*-) after 2 h (Table 2, entry 1). We next tested the addition of 0.2 equivalent of water, which resulted in a significantly improved yield of 85% with a regioselectivity of 41:54:5 (*o*-: *p*-: *m*-) (Table 2, entry 2). With the amount of water increased to 1.2 eq., the yield dropped back to low yield of 43%, which indicated that excessive hydration of BF_3-OEt_2 is disfavorable to this transformation (Table 2, entry 3). Using undistilled toluene under an atmosphere of dry N_2 (moisture content originates from toluene) and anhydrous toluene in air (moisture content originates from air) resulted in yields of 79% and 84% with regioselectivities of 41:53:6 and 42:51:7 (*o*-: *p*-: *m*-), respectively (Table 2, entries 4 and 5). Using open-flask conditions with undistilled toluene, benzyl alcohol gave rise to diphenylmethane in 89% with a regioselectivity of 42:53:5 (*o*-: *p*-: *m*-) (Table 2, entry 6). After the reaction the low layer was analyzed by ^{11}B NMR spectroscopy and a signal at -0.97 ppm (vs. -0.94 ppm) was observed, which suggested the continuous formation of BF_3-H_2O during the benzylation reaction. Other boron compounds were tested as well. BF_3-THF, BF_3-$2H_2O$ and HBF_4-OEt_2[32] provided yields of 82%, 9% and 87% (Table 2, entry 7-9), respectively, whereas H_3BO_3 led to no product formation (Table 2, entry 10). The inferior result of BF_3-$2H_2O$ further showed that excessive hydration of BF_3-OEt_2 was detrimental to this benzylation.

Table 2. Reaction of Benzyl Alcohol with Toluene under Different Conditions.[a]



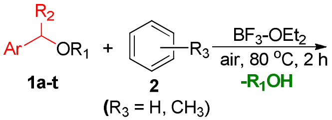
1a **2** **3a**

Entry	Boron sources	H_2O	Atmosphere	Yield (%)[b], ratio (*o*- : *p*- : *m*-)[c]
1[d]	BF_3-OEt_2 (1.2 eq.)	-	N_2	31 (44:48:8)
2[d]	BF_3-OEt_2 (1.2 eq.)	0.2 eq.	N_2	85 (41:54:5)
3[d]	BF_3-OEt_2 (1.2 eq.)	1.2 eq.	N_2	43 (46:49:5)
4	BF_3-OEt_2 (1.2 eq.)	-	N_2	79 (41:53:6)
5[d]	BF_3-OEt_2 (1.2 eq.)	-	air	84 (42:51:7)
6	BF_3-OEt_2 (1.2 eq.)	-	air	89 (42:53:5)
7	BF_3-THF (1.2 eq.)	-	air	82 (40:54:6)
8[d]	BF_3-$2H_2O$ (1.2 eq.)	-	N_2	9 (45:50:5)
9[d]	HBF_4-OEt_2 (1.2 eq.)	-	N_2	87 (39:54:7)
10	H_3BO_3 (1.2 eq.)	-	air	0

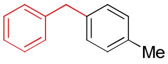
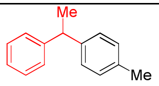
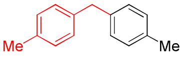
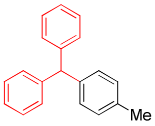
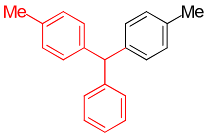
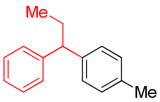
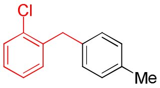
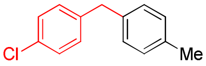
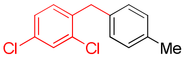
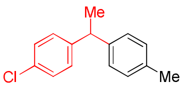
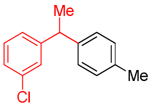
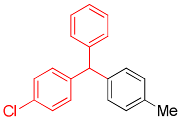
[a] Conditions: benzyl alcohol (1.0 mmol), undistilled toluene (2.0 mL), boron sources (1.2 eq.), 80 °C for 2 h. [b] Yields of isolated products after silica gel column chromatography. [c] Isomer ratios determined by ^{13}C NMR. [d] The reaction was performed in anhydrous toluene.

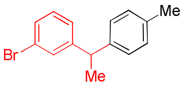
Having explored the reaction conditions, our interest then focused on the influence of the benzyl alcohols and acetate substitution in the Friedel-Crafts reaction with undistilled toluene (Table 3). Using the optimal reaction conditions described above (Table 1, entry 3), the generality of benzyl alcohols and acetates **1** has been investigated. A large variety of primary and secondary benzyl alcohols and acetates were greatly tolerated in this reaction. Throughout, the free alcohols and acetates resulted in very similar reactivity. Both the yields and the regioselectivities were not affected by the choice of precursor. We noted two exceptions: **3r** and **3s**. In the case of **3r**, an increased yield was obtained when using the *bis*-acetate as a benzyl precursor whereas, in the case of **3s**, this was the opposite way and the free alcohol performs much better. In the case of **3r** this difference is readily explained by the poor solubility of the free benzyl alcohol compared to the *bis*-acetate under the reaction conditions. Furthermore, the yields of **3p** and **3q** possessing naphthyl groups are somewhat lower. To our delight this reaction gave excellent yields for a variety of halogenated benzyl donors (**3g-o**) which are amongst the more challenging substrates in benzylation reactions.[17c] The secondary alcohols and corresponding acetates employed predominantly give the expected *para*-substituted products (**3b**, **3d**, **3e**, **3f**, **3j**,**3k**, **3l**, **3m**, **3n** and **3q**) (> 78% regioselectivity). In addition, we do not observe elimination products when using secondary alcohols (**1b**, **1f**, **1j**, **1k**,**1m**,**1n** and **1q**) bearing β-H atoms which can potentially form in the presence of Bronsted and Lewis acids.

Table 3. Scope of BenzylatingAgents.[a]

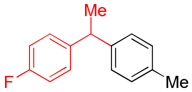


1a-t **2** (R_3 = H, CH_3) **3a-t**

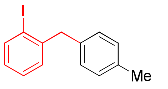
 **3a**[b] R^1 = H, 96% (*o*- : *p*- : *m*- = 41:53:6) R^1 = Ac, 86% (*o*- : *p*- : *m*- = 42:51:7)	 **3b**[b] R^1 = H, 91% (*o*- : *p*- : *m*- = 5:90:5) R^1 = Ac, 89% (*o*- : *p*- = 12:88)	 **3c** R^1 = H, 93%[a] (*o*- : *p*- : *m*- = 4:69:27) R^1 = Ac, 97% (*o*- : *p*- : *m*- = 4:66:30)
 **3d** R^1 = H, 92% (*o*- : *p*- = 9:91) R^1 = Ac, 89% *o*- : *p*- = 13:87	 **3e** R^1 = H, 91% (*o*- : *p*- = 12:88) R^1 = Ac, 96% (*o*- : *p*- = 11:89)	 **3f** R^1 = H, 91% (*o*- : *p*- = 7:93) R^1 = Ac, 89% (*o*- : *p*- = 11:89)
 **3g** R^1 = H, 94% (*o*- : *p*- : *m*- = 42:49:9) R^1 = Ac, 92% (*o*- : *p*- : *m*- = 38:48:14)	 **3h** R^1 = H, 95%(*o*- : *p*- : *m*- = 41:51:8) R^1 = Ac, 95% (*o*- : *p*- : *m*- = 42:44:14)	 **3i** R^1 = H, 97%(*o*- : *p*- : *m*- = 40:45:15) R^1 = Ac, 94% (*o*- : *p*- : *m*- = 40:45:15)
 **3j** R^1 = H, 85% (*o*- : *p*- : *m*-= 9:85:6) R^1 = Ac, 91% (*o*- : *p*- : *m*- = 6:78:16)	 **3k** R^1 = H, 95% (*o*- : *p*- : *m*- = 12:84:4) R^1 = Ac, 88% (*o*- : *p*- : *m*- = 16:80:4)	 **3l** R^1 = H, 98% (*o*- : *p*- = 9:91) R^1 = Ac, 96% (*o*- : *p*- = 11:89)



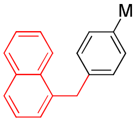
3m
R^1 = H, 84%(*o-* : *p-* : *m-* = 13:83:4)
R^1 = Ac, 91% (*o-* : *p-* : *m-* = 15:80:5)



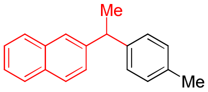
3n
R^1 = H, 84%(*o-* : *p-* : *m-* =9:86:5)
R^1 = Ac,81% (*o-* : *p-* : *m-* = 10:87:3)



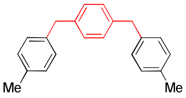
3o
R^1 = H, 91% (*o-* : *p-* : *m-* = 35:53:12)
R^1 = Ac, 91% (*o-* : *p-* : *m-* = 34:53:13)



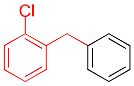
3p
R^1 = H, 71% (*o-* : *p-* = 16:84)
R^1 = Ac, 62% (*o-* : *p-*: *m-* = 17:78:5)



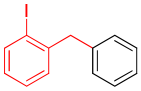
3q
R^1 = H, 59% (*o-* : *p-* = 9:91)
R^1 = Ac, 67% (*o-* : *p-* = 8:92)



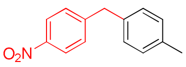
3r[c]
R^1 = H, 32% (*o-* : *p-* : *m-* = 33:62:5)
R^1 = Ac, 85% (*o-* : *p-* : *m-* = 35:60:5)



3s
R^1 = H, 87%
R^1 = Ac, 38%



3t
R^1 = H, 87%

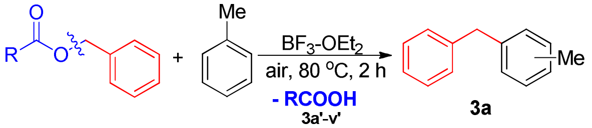


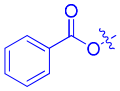
3u[d]
R^1 = H, 21% (*o-* : *p-* : *m-* = 18:41:41)

[a] Conditions:benzylating agent (1.0mmol), BF_3-OEt_2 (1.2 eq.), aromatic (2.0 mL), 80 °C for 2 h in air; yields of isolated products are given and only major products were presented; ratios of isomers aredetermined by ^{13}C NMR.[b]BF_3-OEt_2 (2.0eq.). [c]BF_3-OEt_2 (2.4eq.). [d] BF_3-OEt_2 (4.0 eq.) and toluene (4.0 mL) at 100 °C for 9 h.

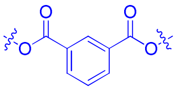
In a further effort we decided to rigorously investigate the effects of the acyl-moiety on the ability to serve as a benzyl donor (Table 4). Without any exception we observe very good reactivity and no significant effects on the regioselectivity. This demonstrates that a benzyliccation is formed which subsequently undergoes an electrophilic aromatic substitution (vide infra). In addition, it should be noted that the carboxylic acids tested possess a wide range of functional groups which are greatly tolerated under the reaction conditions. Therefore, one might consider application of this method as a mild deprotecting strategy. Benzyl esters are normally cleaved via Pd-based hydrogenolysis. In our deprotecting cases, all the benzyl esters were deprotected with a nice finding, and the substrates with nitro,cyano and thiophenegroups (**3g'-i'** and **3q'**) can be utilized to debenzylation directly as well.

Table 4. Benzylation of Toluene with Different Benzyl Carboxylic Ester.[a]

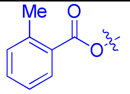




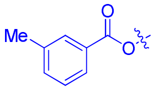
3a, 88% (*o-* : *p-* : *m-* = 40:54:6) (**3a'**, 91%)

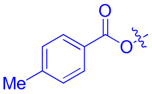


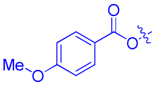
3a, 94% (*o-* : *p-* : *m-* = 41:50:9)(**3b'**, 99%)



3a, 95% (*o-* : *p-* : *m-* = 41:54:5)(**3c'**, 97%)



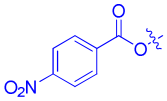




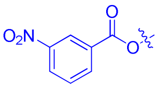
3a, 96% (*o-* : *p-* : *m-* = 40:52:8)(**3d'**, 92%)

3a, 98%, *o-* : *p-* : *m-* = 40:54:6)(**3e'**, 93%)

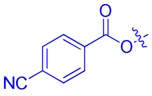
3a, 84% (*o-* : *p-* : *m-* =40:53:7)[b] (**3f'**, 87%)



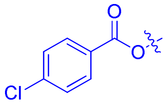
3a, 96% (*o-* : *p-* : *m-* = 41:52:7) (**3g'**, 97%)



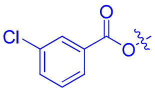
3a, 92% (*o-* : *p-* : *m-* = 43:51:6) (**3h'**, 97%)



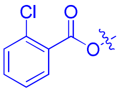
3a, 90% (*o-* : *p-* : *m-* = 41:52:7) (**3i'**, 98%)



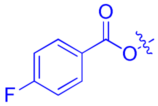
3a, 99% (*o-* : *p-* : *m-* = 40:52:8) (**3j'**, 97%)



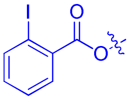
3a, 89% (*o-* : *p-* : *m-* = 41:53:6) (**3k'**, 91%)



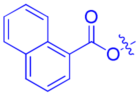
3a, 87% (*o-* : *p-* : *m-* = 43:51:6) (**3l'**, 92%)



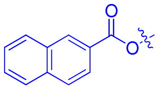
3a, 90% (*o-* : *p-* : *m-* = 41:52:7) (**3m'**, 95%)



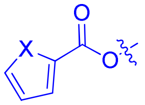
3a, 97% (*o-* : *p-* : *m-* = 42:52:6) (**3n'**, 97%)



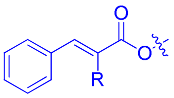
3a, 80% (*o-* : *p-* : *m-* =41:51:8) (**3o'**, 99%)



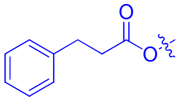
3a, 87% (*o-* : *p-* : *m-* = 39:53:8) (**3p'**, 99%)



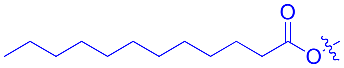
X = S: **3a**, 86% (*o-* : *p-* : *m-* = 41:52:7) (**3q'**, 99%)
X = O: **3a**, 80% (*o-* : *p-* : *m-* = 40:54:6) (**3r'**, 99%)



R = H: **3a**, 90% (*o-* : *p-* : *m-* = 39:54:7) (**3s'**, 93%)
R = Me: **3a**, 87% (*o-* : *p-* : *m-* = 40:53:7) (**3t'**, 98%)



3a, 83% (*o-* : *p-* : *m-* = 39:52:9) (**3u'**, 98%)

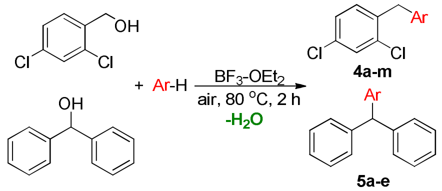


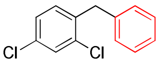
3a, 92% (*o-* : *p-* : *m-* = 40:52:8) (**3v'**, 92%)

[a] Conditions: benzylating agent (1.0 mmol), BF_3-OEt_2 (1.2 eq.), toluene (2.0 mL), 80 °C for 2 h in air; isolated yields for benzyltoluene and carboxylic acids and only major products were presented for benzyltoluene; isomer ratios were determined by ^{13}C NMR. [b] 2.0 Equivalents of BF_3-OEt_2 was used.

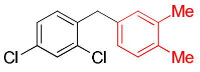
The reactivity of a range of arenes was explored using *ortho*, *para* dichloro benzyl alcohol (**1i**) and diphenyl methanol (**1d**) (Table 5). Benzene gave rise to monobenzylation product **4a** in excellent yield of 93%. Throughout we observe excellent reactivity for electron rich arenes possessing methyl substituents and regioselectivities which match the steric pattern of the starting materials (**4b-4f** and **5a-e**). When using naphthalene $CHCl_3$ was used as a (co)solvent using 4.0 equivalents of the arene obtaining **4g** in 72% isolated yield. Thiophenes could also be employed in this reaction, albeit in a moderate yield (**4i** and **4j**). Electron deficient trifluorotoluene also gave the desired product **4k** in modest 42% yield favoring the *meta*-product as expected, which has the potential to be utilized in modern pharmaceuticals and specialty materials.[33] In this case the reaction temperature had to be raised to 100 °C. Fortunately, dichloroarene gave tetrachloro-substituted diarylmethane (**4m**) in good yield with regioselectivity of above 87%, whereas using monochloroarene led to a closely quantitative transformation (**4l**) with regioslectivity of above 72%.

Table 5.Benzylation of Different Aromatics and only Major Products were Presented.[a]

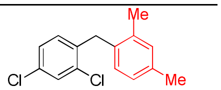




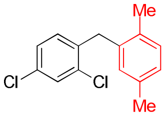
4a, 93%



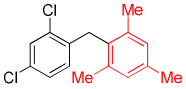
4b, 91% (*3-* : *4-* = 34:66)



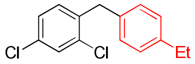
4c, 90% (*2-* : *4-*:*5-* = 16:79:5)



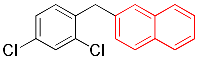
4d, 92%



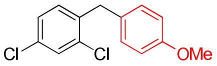
4e, 94%



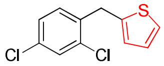
4f, 88% (*o-* : *p-* : *m-* = 38:46:16)



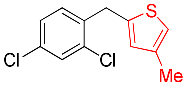
4g, 72%[b] (*1-* : *2-* = 47:53)



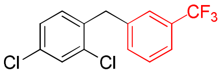
4h, 61% (*p-* >99)



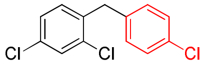
4i, 88% (*3-* : *2-* = 36:64)



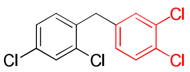
4j, 60% (*4-* : *5-* : *2-* = 16:45:39)



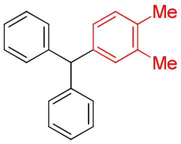
4k, 42%[c] (*m-* > 99)



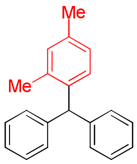
4l, 99%[c] (*o-* : *p-* : *m-* = 24:72:4)



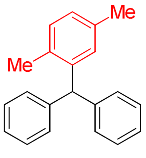
4m, 74%[d] (*3-* : *4-* = 13:87)



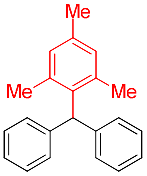
5a, 93% (*3-* : *4-* = 4:96)



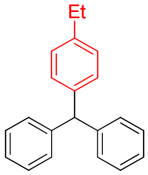
5b, 92%



5c, 86%



5d, 97%



5e, 99% (*o-* : *p-* = 18:82)

[a] Conditions: benzylating agent (**1d** or **1i**, 1.0 mmol), BF_3-OEt_2 (1.2 eq.), aromatics (2.0 mL), 80 °C for 2 h in air; yields of isolated products are provided and only major products were presented; ratios of isomers are determined by ^{13}C NMR. [b] BF_3-OEt_2 (1.2 eq.), aromatics (4.0 eq.), $CHCl_3$ (2.0 mL). [c] BF_3-OEt_2 (4.0 eq.), aromatic (4.0 mL), 100 °C, 2 h. [d] BF_3-OEt_2 (3.0 eq.), aromatic (2.0 mL).

As common Friedel-Crafts reaction of alcohol via an electrophilic substitution of carbonium intermediate in the presence of Lewis acid or Bronsted acid, benzylaiton reaction of benzyl alcohol initially gives rise to the carbonium intermediate in the presence of superacid BF_3-H_2O. The BF_3-OEt_2 has been found a highly-sensitive Lewis acid and hydration reaction might occurs even during the addition of the reagent. As a result, a low reactivity for benzylation was yet obtained in the absence of water under nitrogen atmosphere (Table 2, entry 1). When 0.2 equivalent of water is added, 0.2 equivalent of BF_3-OEt_2 is converted into an equal amount of superacid BF_3-H_2O to promote the benzylation and extra 0.2 equivalent of by–product water is released, which subsequently complexes with another 0.2 equivalent of BF_3-OEt_2 to generate an equal amount of superacid BF_3-H_2O. The by-product water goes and returns in following such a circle until the residual BF_3-OEt_2 is exhausted and the benzylation is complete. In the cases of carboxylic esters, the decomposed carboxylic acid undergoes the similar procedure.

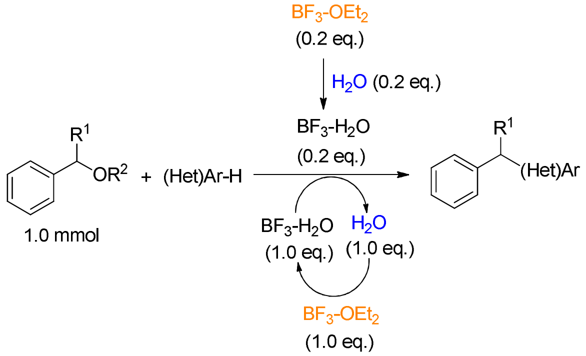


Figure 2. The proposed mechanism.

Conclusions

We have developed a simple and straightforward method for synthesis of diarylalkanes using superacid BF_3-H_2O *in situ* prepared from commercially available BF_3-OEt_2 starting from free benzylic alcohols or acetates. In this work, 39 cases of OH activation using benzyl alcohols as substrates have been demonstrated, and as a comparison of reactivity and regioselectivity benzyl carboxylic esters have been employed and investigated in 39 cases. With a combination of control experiments and ^{11}B NMR analysis, superacid BF_3-H_2O formed in moisture condition as the true promotor has been illuminated. This method is compatible with a number of functional groups and generally gives good to excellent isolated yields. Interestingly, secondary benzyl alcohols as well as arenes bearing electron-withdrawing groups such as triflurometyl and chloro generally result in better regioselectivities.

Experimental

General Methods

All reactions were carried out without any precautions against air and moisture. ^1H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 500 spectrometer at 20-25 °C.^{11}B NMR spectra were recorded on an Agilent 600MR spectrometer at 20-25 °C.^1H NMR spectra were reported in parts per million using TMS (δ = 0.00 ppm) as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were reported in parts per million using solvent $CDCl_3$ (δ = 77.2 ppm) as an internal standard. ^{11}B NMR spectra were reported using saturated aqueous H_3BO_3 solution (δ = 19.49 ppm) as an external standard. Reactions were monitored by TLC. All the reagents used were of analytical grade, purchased locally and used without any purification unless otherwise specified.

Toluene distillation: Toluene purchased from chemical supplier was firstly dried over 4 Å molecular sieve for one week, and then transferred to distillation apparatus under nitrogen protection. Na slice was added, and after reflux for half a day, dry toluene was collected for use.

Typical procedure for benzylation reaction

In a round-bottom flask, phenylmethanol (**1a**, 108.1 mg, 1.0 mmol) and BF_3-OEt_2 (151 μL, 1.2 mmol) were dissolved in toluene (**2**, 2.0 mL). After stirring for 2 h at 80 ^{o}C in atmosphere, the rest toluene was removed under vacuum by a rotary evaporator. The residue was isolated by column chromatography on silica gel using petroleum ether as eluent to give colorless oil**3a**.

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Notes and references

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[‡]These authors contributed equally.

† Electronic Supplementary Information (ESI) available: General information, experimental procedures, characterization data of products and the copies of NMR spectra. See DOI: 10.1039/b000000x/

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