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Direct Syntheses of Diphenylmethanol Derivatives from Substituted Benzenes and $CHCl_3$ through Friedel-Crafts Alkylation and Post-Synthetic Hydrolysis or Alcoholysis Catalyzed by Alumina

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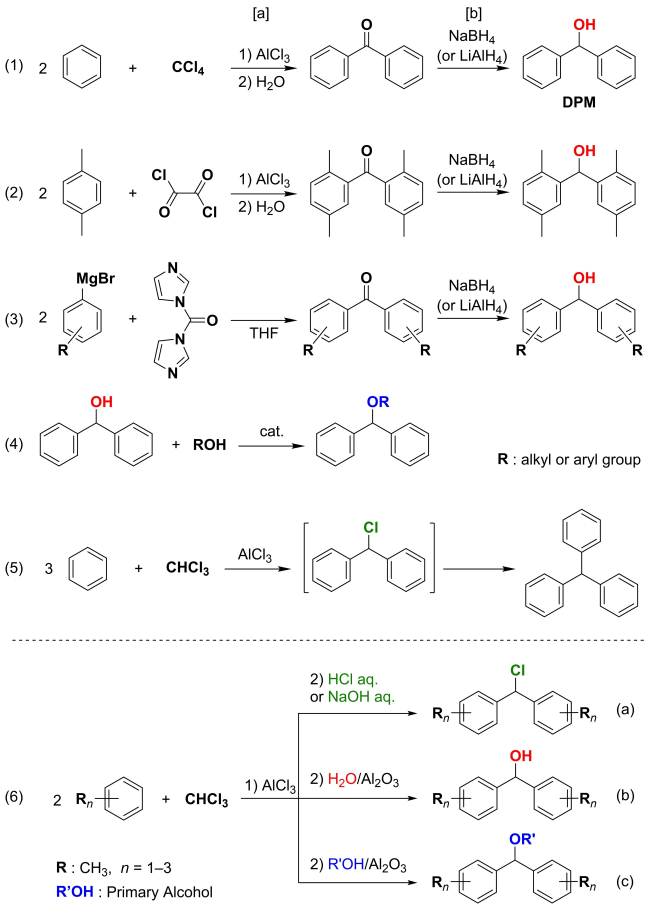
The present study reports an innovative finding that alumina containing water or primary alcohol catalyzes the hydrolysis or alcoholysis, respectively, of the product formed through $AlCl_3$-mediated Friedel-Crafts alkylation of methyl-substituted benzenes and $CHCl_3$. The former and later reactions mainly provided hydroxy- and alkoxy-substituted diarylmethanes, respectively, while the reference reactions without alumina provided bisarylchloromethane. This method enables the selective syntheses of diphenylmethanol derivatives with very simple procedures, without expensive reagents and apparatuses. Furthermore, the alumina used in the reaction could be recycled by washing with water and subsequent drying. From the viewpoint of material recycling, this function is very important for the development of sustainable chemical reactions.

Introduction

Diphenylmethanol (DPM) and its derivatives are important building blocks in manufacturing perfumes, pharmaceuticals, and useful organic chemicals.[1–7] For example, they are utilized for fabricating adrafinil, which acts as a central nervous system stimulant,[1,2] diphenhydramine and diphenylpyralinen having antihistamine effects,[3–5] and cinnarizine as a vasodilator.[6] In practice, DPM is synthesized by the reduction of benzophenone or by a Grignard reaction between phenylmagnesium bromide and benzaldehyde.[8] The former benzophenone is produced by an $AlCl_3$-mediated Friedel-Crafts reaction of benzene and CCl_4, and subsequent hydrolysis of the formed dichlorophenylmethane (Scheme 1, reaction (1)).[9] In recent studies, DPM derivatives have also been synthesized using the corresponding benzophenone derivatives produced from substituted benzenes and oxalyl chloride, or from aryl Grignard reagents and 1,1′-



Scheme 1. Conventional synthetic methods of diarylmethanols (1)–(3) and diarylmethyl ethers (4), Friedel-Crafts reaction of benzene and $CHCl_3$ (5), and new reaction processes developed in this study (6).

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carbonyldiimidazole [Reactions (2) and (3), respectively].[10,11] Subsequent reductions of the benzophenone derivatives provided the corresponding alcohols.[12–15] Furthermore, the resulting OH group on DPM derivatives can be protected by catalytic etherification with alcohols [Reaction (4)].[16–19]

Although reaction (1) may have advantages over other reactions in terms of cost and atom economy, the use of CCl_4 is strictly regulated worldwide in manufacturing production owing to its potential toxicity and environmental concerns. An alternative method using oxalyl chloride, which is more toxic and corrosive, is also unfavorable, especially for large-scale syntheses. Furthermore, the last hydrogenation of the carbonyl group adds one more step to the synthetic process, and uses reactive inorganic reagents such as $NaBH_4$, $LiAlH_4$, and H_2/catalyst, some of which are flammable and corrosive, and, in addition, generate more waste.[12–15] Considering this background, we have studied a novel simple and safe method for synthesizing DPM derivatives without using hazardous and expensive reagents/materials. Here, we report an innovative direct synthetic method of DPM derivatives and their alkyl ethers from methyl-substituted benzenes and chloroform ($CHCl_3$) in high yields through Friedel-Crafts alkylation and post-synthesis treatment with neutral alumina containing water or primary alcohols [Reaction (6)].[20] Alumina has been known to catalyze a variety of chemical reactions, such as oxidation, dehydration, and hydrolysis,[21–23] and it herein enables the catalytic hydrolysis and alcoholysis reactions of the products formed by Friedel-Crafts alkylation.

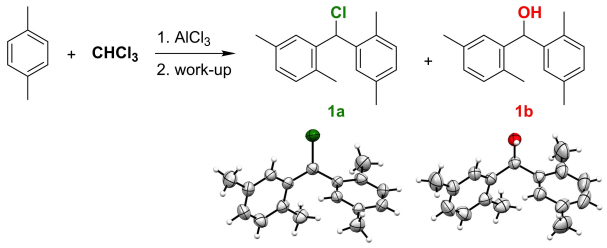
Results and Discussion

Selective Synthesis of Bis(2,5-xylyl)chloromethane 1 a and Bis(2,5-xylyl)methanol 1 b

$CHCl_3$ is a widely used organic solvent, and is also a versatile C1 building block in organic synthesis.[24] It is a raw material for the industrial production of tetrafluoroethylene (TFE), and is also used as a precursor of carbene and phosgene, which have high reactivities.[25,26] Furthermore, it is known that $CHCl_3$ reacts with three equivalents of benzene though a Friedel-Crafts reaction mediated by $AlCl_3$ to give triphenylmethane [Scheme 1, reaction (5)].[27] A possible mechanism for this reaction is the formation of chlorodiphenylmethane as an intermediate.[28] With an expectation to obtain this intermediate compound, we carried out an $AlCl_3$-mediated Friedel-Crafts alkylation of benzene with a larger amount of $CHCl_3$. When $AlCl_3$ (8 mmol) was added to a 1:46 mixed solution of benzene and $CHCl_3$ (8 and 370 mmol, respectively), and stirred at 0 °C for 6 h, the reaction occurred with generation of HCl gas to mainly give insoluble black precipitates. Hypothesizing that the reaction provided polymeric products having complicated structures, we performed the reaction with a mixture of *p*-xylene and $CHCl_3$ at 0 °C for 6 h. With this combination, the reaction occurred, without precipitation, to give bis(2,5-xylyl)chloromethane **1 a** and bis(2,5-xylyl)methanol **1 b** in 86% and 2% yields, respectively, after quenching the reaction with water at room temperature (Table 1, entry 1). No notable changes for the yield of **1 a** and **1 b** were observed when using either acidic and alkaline water in the post-synthesis work-up (Entries 2–4). Single-crystal X-ray structures of **1 a** and **1 b** (Table 1, header) showed that they adopted conformations that reduced steric repulsion among the methyl groups on the phenyl rings and the Cl or OH group attached to the methylene bridge.

We serendipitously found that the yield of **1 b** was dramatically increased with a concomitant decrease in the yield of **1 a** when quenching the reaction with direct addition of commercially available alumina (Al_2O_3) that contained ≈1.0 wt% water. The resulting solid-liquid mixture was filtered and washed with a dry $CHCl_3$/EtOAc (1:1) solvent mixture. ^{1}H NMR spectroscopic analysis of the combined filtrate showed that **1 b** was formed in 76% yield without **1 a**. To simplify the work-up process, the same sample solution prepared was then directly transferred to an open column containing alumina

Table 1. Reacttion and work-up conditions for synthesizing **1 a** and **1 b**.[a]



Entry	Temp. [°C]	Time [h]	Xylene [mmol]	$AlCl_3$ [mmol]	Work-up[b]	Yield [%][c] 1 a	1 b
1	0	6	8	8	H_2O	86	2
2	0	6	8	8	HCl aq. (0.1 M)	92	1
3	0	6	8	8	HCl aq. (1.0 M)	85	1
4	0	6	8	8	NaOH aq. (0.1 M)	86	2
5	0	6	8	8	Al_2O_3/H_2O (≈1.0 wt%)	2	94
6	0	4	8	8	Al_2O_3/H_2O (≈1.0 wt%)	10	80
7	0	2	8	8	Al_2O_3/H_2O (≈1.0 wt%)	17	70
8	−10	2	8	8	Al_2O_3/H_2O (≈1.0 wt%)	75	10
9	10	2	8	8	Al_2O_3/H_2O (≈1.0 wt%)	1	7
10	0	6	80	80	Al_2O_3/H_2O (≈1.0 wt%)	–	70[d]
11	0	6	8	8	Al_2O_3/H_2O (calcinated)	33	–
12	0	6	8	8	Al_2O_3/H_2O (≈3.6 wt%)	–	81
13	0	6	8	0.8	Al_2O_3/H_2O (≈1.0 wt%)	–	2

[a] Standard conditions: Entries 1–9 and 11–13: $CHCl_3$ (0.37 mol, 30 mL); entry 10: $CHCl_3$ (3.7 mol, 300 mL). Thermal ellipsoids of molecular structures are drawn at the 50% probability level; [b] work-up: room temperature, water, HCl aq. (0.1 or 1.0 M), NaOH aq. (0.1 M), commercially available alumina containing ≈1.0 wt% water (entries 5–9 and 13: 75 g, entry 10: 750 g), dry alumina calcinated at 300 °C (75 g), or wet alumina containing 3.6 wt% water (75 g); [c] yields were estimated from ^{1}H NMR spectroscopic analysis of isolated mixtures of the products; [d] isolated yield.

powder. The mixture immediately soaked into the alumina and generated HCl gas. The sample was then subjected to column chromatography with a dry $CHCl_3$/EtOAc (1:1) solvent mixture to give **1a** and **1b** in 2% and 94% yields, respectively (Entry 5). The combined yields of **1a** and **1b** decreased from 96% to 90% and 87% when decreasing the reaction time from 6 to 4 and 2 h, respectively (Entries 6 and 7). The product ratio of **1b** to **1a** also decreased from 94:2 to 80:10 and 70:17, respectively. The yield of the products was highly dependent on the reaction temperature. When the reaction was conducted at −10 °C for 2 h, the yield of **1b** was decreased to 10% and that of **1a** increased to 75% (Entry 8) without notable change in their combined yields. In contrast, upon elevating the reaction temperature to 10 °C, both the yields of **1a** and **1b** were dramatically decreased to give complicated product mixtures (Entry 9). Since $AlCl_3$ is known to cause not only Friedel-Crafts alkylation but also oxidation reactions, the products might contain larger oligomers and fused aromatic compounds. These experimental results revealed that **1b** was selectively obtained at 0 °C. With the optimized conditions identified above, we then demonstrated a scale-up synthesis with 10 times the amounts of all reagents and solvent (80 mmol of *p*-xylene and $AlCl_3$, and 300 mL of $CHCl_3$), and obtained **1b** in 70% yield (Entry 10).

We then investigated the reactions by varying the water content of alumina, which could be estimated from the difference in weight between calcinated and wet alumina. Alumina adsorbs moisture from the air. In fact, the commercially available alumina used in the reactions of entries 5–9 (75 g for each reaction) was noted to contain ≈1.0 wt% water (see above). The reaction was then conducted with dry alumina prepared through calcination at 300 °C (Figure S1, Supporting Information). Expectedly, only **1a** was obtained in 33% yield without **1b** (Entry 11), even with the same conditions as entry 5 with the best yield of **1b**. The observed low yield of **1a** may result from strong adsorption of the ionic complex on the alumina surface. However, when using wet alumina containing ≈3.6 wt% water, **1b** was obtained in 81% yield without **1a** (Entry 12). Thus, the yield of **1a** decreased and that of **1b** was increased using alumina with a higher water content. These experimental results indicate that the alumina works as a solid catalyst for the hydrolysis reaction of the ionic complex (**III**) to the corresponding diarylmethanol. However, when using a catalytic amount of $AlCl_3$ (0.1 equiv.) for quenching the reaction, **1b** was obtained only in 2% yield (Entry 13).

The alumina used in the reaction could be recycled for use in the same reaction by washing with water and drying (Figure 1A). The adsorbed compounds, salts, and solvent remaining on the alumina were washed away with water; then, the wet alumina was dried at 120 °C for 1 h, and then at 300 °C for 3.5 h to reproduce dry alumina. The recycled alumina could be reused for the catalytic hydrolysis reaction over and over again in the work-up process. No notable changes in the yields of **1a** and **1b** were observed for a total of five repetitions (Figure 1B). Total weight loss for the recycled alumina was only 4%, likely due to technical loss.

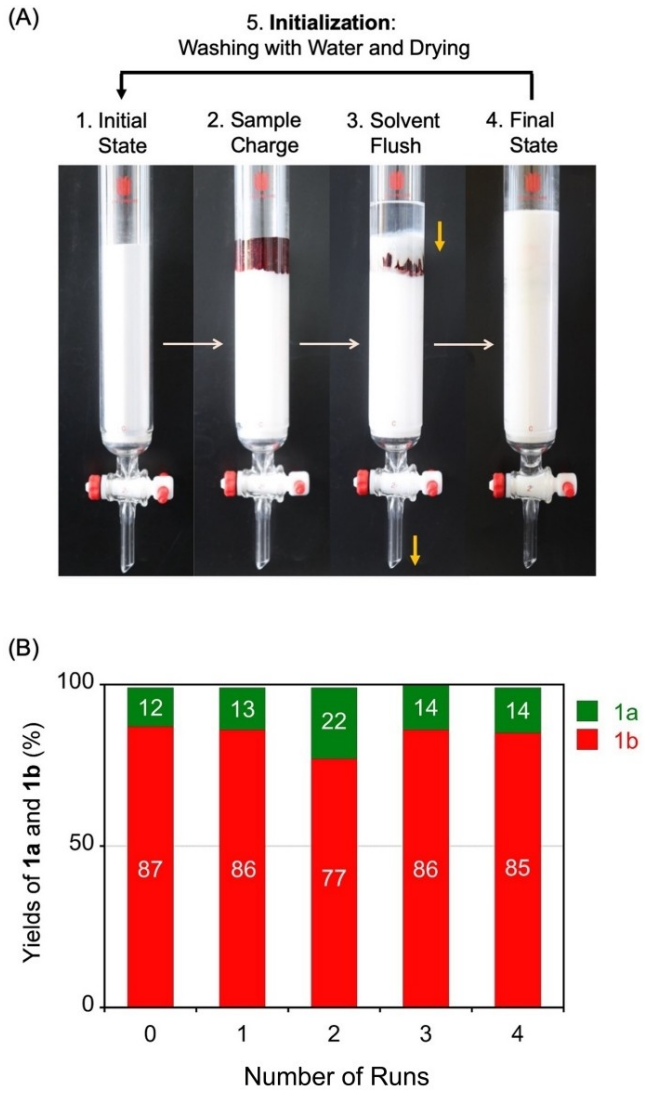
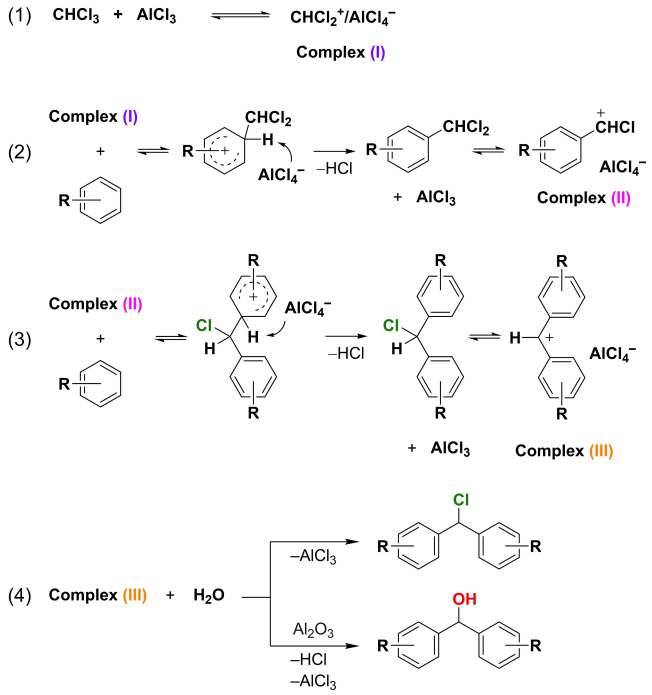


Figure 1. Recyclability of alumina in synthesizing bis(2,5-xylyl)chloromethane (**1a**) and bis(2,5-xylyl)methanol (**1b**). (A) Work-up of the product formed upon $AlCl_3$-mediated Friedel-Crafts alkylation with alumina and initialization of the used alumina; (B) yields of **1a** and **1b** with respect to the number of recycling runs; standard conditions: *p*-xylene (8 mmol), $AlCl_3$ (8 mmol, 1 equiv.), $CHCl_3$ (370 mmol, 30 mL), 0 °C, 6 h; work-up: wet recycled alumina (water content 4.6 wt%). Yields (green, **1a**; red, **1b**) were estimated from ^{1}H NMR spectroscopic analysis of isolated mixtures of the products.

Mechanism of the Reactions and Work-Up with the Alumina

A plausible reaction mechanism for formation of the diarylmethanol is shown in Scheme 2. $AlCl_3$ generally brings about Friedel-Crafts alkylation of benzene and $CHCl_3$ to give triphenylmethane through the formation of ionic complexes (**I**), (**II**), and (**III**) (Reactions 1–3, respectively).[28,29] However, under our conditions ([$CHCl_3$] > [aryl substrate] = [$AlCl_3$] and 0 °C), the reaction may be terminated at complex (**III**), whose positive charge at the chloromethylene bridge is delocalized over the two aromatic rings to stabilize the ionic structure. The observed time- and temperature-dependences of the yields of **1a** and **1b** shown in Table 1 (Entries 5–9) may result from the amount of complex (**III**) formed. Water then breaks complex (**III**) to give



Scheme 2. Possible reaction mechanism for formation of diarylmethanols.

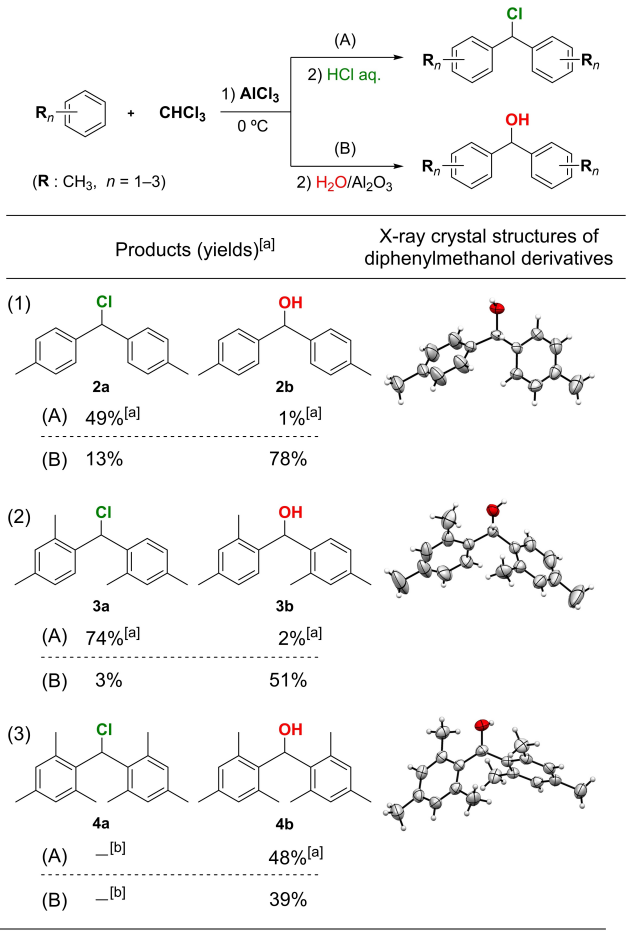


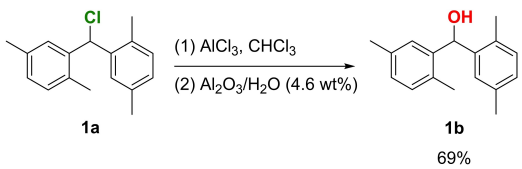
Figure 2. Selective syntheses of diarylchloromethanes and diarylmethanols by post-synthesis work-up with (A) 0.1 M HCl aq. or (B) alumina containing ≈1.0 wt% water; standard conditions: methyl-substituted benzene (8 mmol), $AlCl_3$ (8 mmol, 1 equiv.), $CHCl_3$ (370 mmol, 30 mL), 0 °C, 6 h; thermal ellipsoids of molecular structures are drawn at the 50% probability level for **2b** and **4b**, and at the 30% probability level for **3b**; [a] yields were estimated from ^{1}H NMR spectroscopic analysis using 1,2-dichloroethane as an internal standard; [b] not found.

diarylchloromethane, while the alumina promotes the catalytic hydrolysis reaction to give diarylmethanol (Reaction 4).

Correspondingly, the catalytic hydrolysis reaction on the alumina surface can be explained as follows: Brönsted and/or Lewis acid points of the alumina may strongly interact with anionic $AlCl_4^-$ to accelerate the substitution reaction of H_2O to complex (**III**), the cationic counterpart. In contrast, adsorption of water molecules onto the alumina may decelerate the hydrolysis of $AlCl_4^-$. In support of this proposed mechanism, **1a** was actually converted to **1b** in 69% yield upon mixing with $AlCl_3$ in $CHCl_3$ and subsequent hydrolysis with wet alumina (Scheme 3).

Synthesis of a Series of Diarylmethanols

Next, we applied this reaction to a series of methyl-substituted benzenes (toluene, *m*-xylene, and 1,3,5-trimethylbenzene) (Figure 2). An $AlCl_3$-mediated reaction of toluene with $CHCl_3$ after post-synthesis hydrolysis with aqueous HCl or wet alumina mainly provided the corresponding 4-substituted diarylchloromethane **2a** in 49% yield, or diarylmethanol **2b** in 78% yield, respectively. *m*-Xylene, having two methyl groups, also provided the corresponding product **3a** in 74% yield or **3b** in 51% yield, respectively, after the hydrolysis using the same procedure. However, 1,3,5-trimethylbenzene, having three methyl groups, gave **4b** in low yields using both post-synthesis hydrolysis methods without the expected **4a**. This may be due to the structure and reactivity of the resulting complex (**III**). As observed for the X-ray crystallographic structures of **3b** and **4b**, substituents on the methylene bridge are sterically crowded by the multiple methyl groups on the phenyl ring. Three methyl groups attached to the phenyl ring may thus, for steric reasons, decelerate electrophilic substitutions of the complexes (**I**) and (**II**) to another aromatic substrate, resulting in a decrease in product yield. However, the methyl groups may electronically and sterically stabilize the resulting diphenylmethyl cation in complex (**III**), accelerating the reaction to form **4b**.



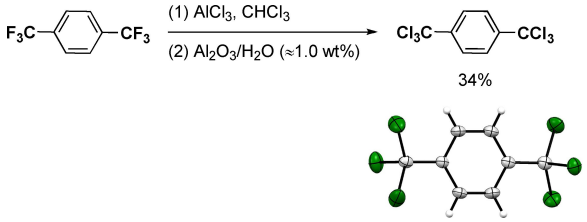
Scheme 3. Reference reaction of **1a** with $AlCl_3$ in $CHCl_3$ and post-synthesis work-up with wet alumina; conditions: **1a** (1.4 mmol), $AlCl_3$ (1.4 mmol, 1 equiv.), $CHCl_3$ (190 mmol, 15 mL), 0 °C, 6 h; work-up: alumina containing 4.6 wt% water.

The reaction was then carried out for the benzene derivatives by varying substituent groups to investigate the

versatility of the present reaction. 1,4-Diethylbenzene, having ethyl groups and thus larger than the methyl derivatives, showed no reaction. 1,4-Dimethoxybenzene and 1,4-diiodobenzene, containing electron-donating methoxy groups and electron-withdrawing iodide groups, respectively, also showed no reactions. Although 1,4-bis(trifluoromethyl)benzene also did not provide the corresponding diarylmethanol, it underwent a fluorine-to-chlorine substitution to give 1,4-bis(trichloromethyl)benzene in 34% yield (Scheme 4).[30] Anthracene, having multiple reactive positions, showed complicated product mixtures. These results indicates that the present reaction is specifically available to methyl-substituted benzenes.

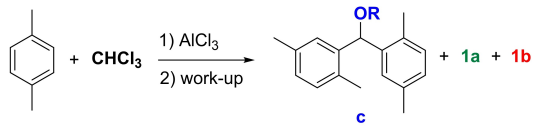
Syntheses of Diarylmethyl Ethers

Based on these results and the reaction mechanism discussed above, we next investigated if *O*-alkylation was possible through post-synthesis alcoholysis with alumina containing primary aliphatic alcohols (Table 2). As observed in the case with water for the post-synthesis hydrolysis reaction without alumina, *p*-xylene only provided **1a** through an $AlCl_3$-mediated Friedel-Crafts reaction with $CHCl_3$ and work-up with MeOH.



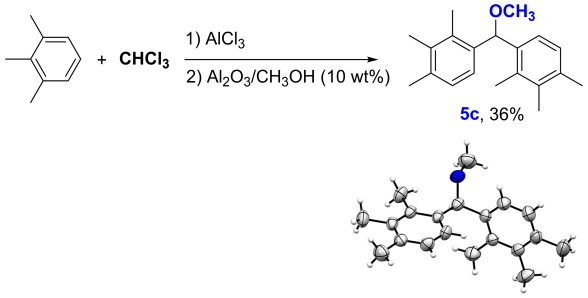
Scheme 4. Reaction of 1,4-bis(trifluoromethyl)benzene with $AlCl_3$ in $CHCl_3$ and post-synthesis work-up with alumina containing ≈1.0 wt% water; standard conditions: 1,4-bis(trifluoromethyl)benzene (8 mmol), $AlCl_3$ (8 mmol, 1 equiv.), $CHCl_3$ (370 mmol, 30 mL), 0 °C, 6 h; thermal ellipsoids for 1,4-bis(trichloromethyl)benzene are drawn at the 50% probability level.

Table 2. Syntheses of diarylmethyl ethers by post-synthesis work-up with alumina containing an alcohol.[a]



Entry	Alcohol content [wt%]	Work-up[b]	Yield [%][c] c	1a	1b
1	6	Al_2O_3/CH_3OH (6 wt%)	70	13	7
2	10	Al_2O_3/CH_3OH (10 wt%)	81	6	3
3	10	$Al_2O_3/CH_3(CH_2)_5OH$ (10 wt%)	29	4	7
4	10	$Al_2O_3/(CH_3)_2CHOH$ (10 wt%)	–	65	4
5	10	$Al_2O_3/(CH_3)_3COH$ (10 wt%)	–	55	27
6	10	Al_2O_3/PhOH (10 wt%)	–	–	–
7	10	Al_2O_3/CCl_3CH_2OH (10 wt%)	24	20	40
8	10	Al_2O_3/CF_3CH_2OH (10 wt%)	–	3	–

Standard conditions: methyl-substituted benzene (8 mmol), $AlCl_3$ (8 mmol, 1 equiv.), $CHCl_3$ (370 mmol, 30 mL), 0 °C, 6 h; [b] alumina exposed to an alcohol mist (6–10 wt%); [c] yields were estimated from ^{1}H NMR spectroscopic analysis of isolated mixtures of the products.



Scheme 5. Reaction of 1,2,3-trimethylbenzene with $AlCl_3$ in $CHCl_3$ and post-synthesis work-up with alumina containing 10 wt% MeOH; standard conditions: 1,2,3-trimethylbenzene (8 mmol), $AlCl_3$ (8 mmol, 1 equiv.), $CHCl_3$ (370 mmol, 30 mL), 0 °C, 6 h; thermal ellipsoids for **5c** are drawn at the 50% probability level.

However, when the work-up was carried out with alumina containing 6 wt% MeOH, the *O*-methylated product **1c** (R = CH_3) was obtained in 70% yield with minor products **1a** and **1b** in 13% and 7% yield, respectively (Entry 1). The ^{1}H NMR spectrum of **1c**, together with results from HPLC analysis, indicated that **1c** is a mixture of conformers in which rotation of the dimethylphenyl rings is highly restricted by the attached methoxy group on the methylene bridge (Figure S2). In contrast, 1,2,3-trimethylbenzene, which allows substitutions mainly at the 4-position, provided **5c** in 36% yield without such conformers (Scheme 5). The yield of **1c** was further increased to 81% at the expense of other products when increasing the amount of MeOH in the alumina to 10% (Entry 2). With the same procedure as for entry 2, *n*-hexanol having a long alkyl chain provided the corresponding ether in 29% yield (Entry 3). Here, the observed low yield of ether may result from elution of *n*-hexanol from the alumina with the solvent used in chromatography. No alcoholysis occurred with 2-propanol and *tert*-butanol having sterically congested structures (Entries 4 and 5, respectively) and with phenol having lower nucleophilicity (Entry 6). With respect to halogen-substituted alcohols having lower nucleophilicity than the corresponding alkyl alcohols, 2,2,2-trichloroethanol provided the ether in 24% yield, whereas 2,2,2-trifluoroethanol did not provide the ether at all (Entries 7 and 8, respectively).

Conclusion

In conclusion, we have directly synthesized diphenylmethanol derivatives and their alkyl ethers from methyl-substituted benzenes and $CHCl_3$ through $AlCl_3$-mediated Friedel-Crafts alkylation and post-synthesis work-up with alumina containing water or a primary alcohol. The alumina catalyzed the hydrolysis and alcoholysis reactions of a complex of diarylchloromethane and $AlCl_3$ to give the corresponding hydroxy- and alkoxy-substituted diarylmethanes, respectively. The reactions developed in this study are very simple and do not require the use of expensive reagents and apparatuses, and allow recycling of the alumina through washing by water and drying. These reactions are expected to benefit a variety of organic syntheses in both

academia and industry in terms of efficiency, safety, cost, and environmental impact.

Experimental Section

General Information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Neutral aluminum oxide purchased from Tianjin jingdongtianzheng Precision Chemical Reagent Factory (100 mesh, water content ≈1 wt%, pH 6.5–7.5) was used for the work-up process. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE 600 spectrometer where chemical shifts (δ in ppm) were determined with respect to tetramethylsilane as an internal standard. High resolution mass spectrometry (HRMS, ESI-Orbitrap) was performed on a Thermo Fisher Scientific Q Exactive mass spectrometer. High Performance Liquid Chromatography (HPLC) were performed at 25 °C on a Tnature C18 (4.6 mm × 250 mm × 5 μm) column using a Waters E2695 solvent pump, equipped with Waters 2998 PDA detector with CH_3CN/H_2O (9:1) as an eluent. The single-crystal X-ray diffraction data of single crystals were collected on a Bruker SMART APEX CCD area-detector diffractometer with graphite-monochromated Mo*Kα* radiation (λ = 0.71073 Å). The data were collected at 293, 273, or 296 K, and the structures were solved by direct methods using SHELXTL and non-hydrogen atoms were refined by full-matrix least-squares on F^2 using SHELX97. Single crystals of **1a**, **4b** and **5c** were prepared through recrystallization from CH_2Cl_2/MeOH. Single crystals of **1b**, **2b** and **3b** were prepared through recrystallization from *n*-hexane.

Deposition Numbers 2075469 (for **1a**), 2075463 (for **1b**), 2094220 (for **2b**), 2075468 (for **3b**), 2075465 (for **4b**), 2075464 (for 1,4-bis(trichloromethyl)benzene), and 2075466 (for **5c**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

General Procedure 1: Synthesis of Diphenylchloromethane Derivatives

$AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and an aromatic substrate (8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was poured into HCl aq. (0.1 M) at room temperature and stirred for 1 h. It was extracted with $CHCl_3$ (20 mL × 3). The organic layers were combined, dried over anhydrous K_2CO_3, and evaporated to dryness under reduced pressure. The residue was washed with *n*-hexane to give the corresponding diphenylchloromethane derivatives.

General Procedure 2: Synthesis of Diphenylmethanol Derivatives

$AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and an aromatic substrate (8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was dropped onto a commercially available neutral alumina column (water content ≈1 wt%), and subjected to column chromatography with a dry $CHCl_3$/ethyl acetate (1:1) as an eluent. The sample solution collected was evaporated to dryness under reduced pressure, and the residue was recrystallized with *n*-hexane or CH_2Cl_2/methanol to give the corresponding diphenylmethanol derivatives.

General Procedure 3: Synthesis of *O*-Alkylated Diphenylmethanol Derivatives

$AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and an aromatic substrate (8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was dropped onto a neutral alumina column (alcohol content 10 wt%), and subjected to column chromatography with a dry $CHCl_3$/ethyl acetate (1:1) as an eluent. The sample solution collected was evaporated to dryness under reduced pressure, and the residue was subjected to recrystallization or silica gel column chromatography to give the corresponding *O*-alkylated diphenylmethanol derivatives.

2,2′-(Chloromethylene)bis(1,4-dimethylbenzene) (1a): $AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and *p*-xylene (1 mL, 8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was poured into HCl aq. (0.1 M) at r.t. and stirred for 1 h. It was extracted with $CHCl_3$ (20 mL × 3). The organic layers were combined, dried over anhydrous K_2CO_3, and evaporated to dryness under reduced pressure. ^{1}H NMR spectroscopy revealed that the residue contained **1a** in 92% yield. The residue was washed with *n*-hexane for several times to give **1a** as a white solid (0.49 g, 1.9 mmol, 47%).

Bis(2,5-dimethylphenyl)methanol (1b): $AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and *p*-xylene (1 mL, 8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was dropped onto a commercially available neutral alumina column (water content ≈1 wt%), and subjected to column chromatography with a dry $CHCl_3$/ethyl acetate (1:1) as an eluent. The sample solution collected was evaporated to dryness under reduced pressure. ^{1}H NMR spectroscopy revealed that the residue contains **1b** in 94% yield. The residue was recrystallized from *n*-hexane to give **1b** as a white solid (0.76 g, 3.2 mmol, 79%).

2,2′-(Methoxymethylene)bis(1,4-dimethylbenzene) (1c): $AlCl_3$ (1.1 g, 8 mmol) was added to a mixture of $CHCl_3$ (30 mL, 0.37 mol) and *p*-xylene (1 mL, 8 mmol) at 0 °C, and then, the sample solution was stirred for 6 h. Gaseous HCl generated from this reaction system was trapped outside with water containing a base such as K_2CO_3. The resulting sample solution was dropped onto a neutral alumina column (MeOH content 10 wt%), and subjected to column chromatography with dry $CHCl_3$/ethyl acetate (1:1) as an eluent. The sample solution collected was evaporated to dryness under reduced pressure, and the residue was subjected to silica gel column chromatography (CH_2Cl_2) to afford **1c** as a yellow oil (0.82 g, 3.2 mmol, 81%).

Bis(4-methylphenyl)methyl chloride (2a): Since the reaction product prepared from toluene contained some side-products, from which bis(4-methylphenyl)methyl chloride (**2a**) could not be separated by the recrystallization, vacuum distillation, and chromatography, its amount was estimated in ^{1}H NMR spectroscopy with its standard prepared by the literature method.[31] The ^{1}H NMR spectrum is shown in Figure S16. All ^{1}H NMR and ^{13}C NMR data are in agreement with the literature.[32]

Bis(4-methylphenyl)methanol (2b): The compound was synthesized according to the general procedure 2 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and toluene (0.85 mL, 8 mmol). A white solid (0.66 g, 3.0 mmol, 78%) was obtained through recrystallization from *n*-hexane.

4,4′-(Chloromethylene)bis(1,3-dimethylbenzene) (3a): Since the reaction product prepared from *m*-xylene contained some side products, from which 4,4′-(chloromethylene)bis(1,3-dimethylbenzene) (**3a**) could not be separated by recrystallization, vacuum distillation, and chromatography, its amount was estimated by ^{1}H NMR spectroscopy with its standard prepared by the literature method.[31] ^{1}H and ^{13}C NMR spectra are shown in Figures S19 and S20.

Bis(2,4-dimethylphenyl)methanol (3b): The compound was synthesized according to general procedure 2 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and *m*-xylene (1 mL, 8 mmol). A white solid (0.49 g, 2.0 mmol, 51%) was obtained through recrystallization from *n*-hexane.

Bis(2,4,6-trimethylphenyl)methanol (4b): **Method 1**: The compound was synthesized according to general procedure 2 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and 1,3,5-trimethylbenzene (1 mL, 8 mmol). A white solid (0.42 g, 1.6 mmol, 39%) was obtained through recrystallization from CH_2Cl_2/methanol. **Method 2**: The compound was synthesized according to general procedure 1 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and 1.3.5-trimethylbenzene (1 mL, 8 mmol). ^{1}H NMR spectroscopy revealed that the resulting residue contained **4b** in 48% yield. The residue was recrystallized from CH_2Cl_2/methanol to give **4b** as a white solid (0.37 g, 1.4 mmol, 35%).

4,4′-(Methoxymethylene)bis(1,2,3-trimethylbenzene) (5c): The compound was synthesized according to general procedure 3 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and 1,2,3-trimethylbenzene (1 mL, 8 mmol), and post-synthesis work-up with alumina (MeOH content 10 wt%). A yellow solid (0.41 g, 1.4 mmol, 36%) was obtained through recrystallization from CH_2Cl_2/methanol.

2,2′-((Hexyloxy)methylene)bis(1,4-dimethylbenzene): The compound was synthesized according to general procedure 3 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and *p*-xylene (1 mL, 8 mmol), and post-synthesis work-up with alumina (*n*-hexanol content 10 wt%). The collected sample solution was evaporated to dryness under reduced pressure, and the residue was subjected to silica gel column chromatography (CH_2Cl_2) to afford 2,2′-((hexyloxy)methylene)bis(1,4-dimethylbenzene) as a yellow oil (0.38 g, 1.2 mmol, 29%).

2,2′-((2,2,2-Trichloroethoxy)methylene)bis(1,4-dimethylbenzene): The compound was synthesized according to general procedure 3 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and *p*-xylene (1 mL, 8 mmol), and post-synthesis work-up with alumina (2,2,2-trichloroethanol content 10 wt%). The collected sample solution was evaporated to dryness under reduced pressure, and the residue was subjected to silica gel column chromatography (CH_2Cl_2) to afford 2,2′-((2,2,2-trichloroethoxy)methylene)bis(1,4-dimethylbenzene) as a yellow oil (0.36 g, 1.0 mmol, 24%).

1,4-Bis(trichloromethyl)benzene: The compound was synthesized according to general procedure 2 with $AlCl_3$ (1.1 g, 8 mmol), $CHCl_3$ (30 mL, 0.37 mol), and 1,4-bis(trifluoromethyl)benzene (1.24 mL, 8 mmol). Colorless sheet-like crystals (0.39 g, 1.2 mmol, 34%) were obtained through recrystallization from CH_2Cl_2/MeOH.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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