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Convenient synthesis of triarylmethanes and 9,10-diarylanthracenes by alkylation of arenes with aromatic aldehydes using acetyl bromide and $ZnBr_2/SiO_2$

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Abstract

Reaction of electron-rich arenes with acetyl bromide and aldehydes in the presence of silica gel-supported zinc bromide was carried out in benzene to give selectively the corresponding triarylmethanes or 9,10-diarylanthracenes in high yields depending upon the ratio of an arene and an aldehyde. The mild conditions employed are especially noteworthy.

Keywords: Triarylmethane; Anthracene; Aldehyde; Silica gel-supported zinc chloride

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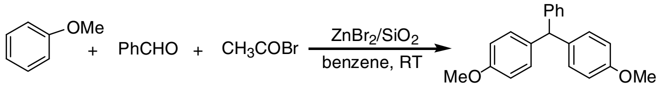
The acid-catalyzed Friedel–Crafts alkylation of arenes with aromatic aldehydes has been known since 1886.[1] The reaction using Lewis acid such as $AlCl_3$ had not received much attention until recently because of the formation of many products such as triarylmethanes, triarylmethanol, diarylmethane, and anthracene derivatives.[2] However, the analogous reaction of aldehydes has been investigated extensively. Lewis acid-catalyzed reductive Friedel–Crafts reaction of arenes with aromatic aldehydes afforded exclusively the corresponding diarylmethanes. For instance, diarylmethanes formed selectively in the reaction using $CaCl_2$,[3] $Sc(OTf)_3$/1,3-propanediol,[4] and $InCl_3$/chloromethylsilane.[5] Recently, it has been reported that the alkylation of arenes with aldehydes using catalytic $AuCl_3/3AgOTf$ [6] or $[Ir(COD)Cl_2/SnCl_4$[7] gives triarylmethanes selectively. $LnCl_3$ (Ln = Pr, Dy, Er, Sm. Yb) and $Yb(OTf)_3$-catalyzed alkylation of PhR (R = H, Me) with AcCl–PhCHO also affords the corresponding triarylmethane.[8] We found that silica gel-supported zinc bromide ($ZnBr_2/SiO_2$) catalyzed alkylation of electron-rich arenes with acetyl bromide–aromatic aldehydes gave the corresponding triarylmethanes in high yields under mild conditions. Triarylmethanes have attracted the attention of chemists because of the interesting properties associated with their derivatives.[9] Although a number of methods are available for the synthesis of triarylmethanes, most of them are multistep process and/or require hash reaction conditions.[10] We wish to report herein a convenient and practical method for the preparation of triarylmethanes and 9,10-diarylanthracenes by the reaction of electron-rich arenes with AcBr and aromatic aldehydes in the presence of $ZnBr_2/SiO_2$. The reaction of anisole with benzaldehyde was carried out in the presence of $ZnBr_2/SiO_2$ at room temperature, but no products were obtained and anisole was recovered. In contrast, the reaction with AcBr and benzaldehyde in the presence of $ZnBr_2/SiO_2$ under similar conditions afforded 4,4′-dimethoxytriphenylmethane **1** in high yield.



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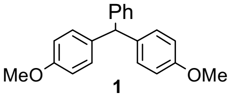
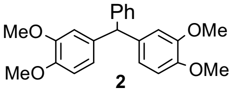
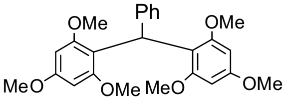
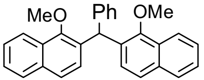
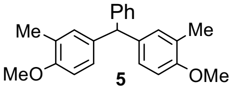
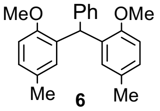
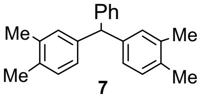
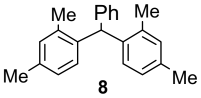
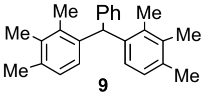
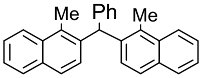
Thus, to a mixture of anisole (4 equiv), benzaldehyde (1 equiv), and $ZnBr_2/SiO_2$[11] in benzene was added dropwise, with stirring, a solution of acetyl bromide in benzene. After the addition, the slurry was stirred for 1 h at room temperature, and **1** was obtained in 84% yield. Acetylanisole which is formed from Friedel–Crafts acylation of anisole with acetyl bromide was not detected. Toluene can also be used as a solvent, whereas in polar solvent such as THF and dioxane the yield is very low. We next explored the bisarylation of benzaldehyde with various arenes for the synthesis of triarylmethanes.[12] The results are shown in Table 1.

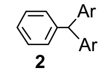
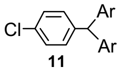
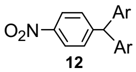
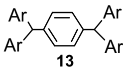
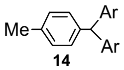
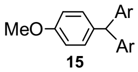
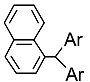
Electron-rich arenes such as anisole, 1,2-dimethoxybenzene (veratrole), 1,3,5-trimethoxybenzene, 2- and 4-methoxytoluene, and 1-methoxynaphthalene gave the corresponding triarylmethane in high yields (entries 1–6).

Table 1
Reaction of various arenes with AcBr and benzaldehyde (PhCHO) leading to triarylmethanes[a]

Entry	Arene	Temp (°C)/time (h)	Product	Yield[b] (%)
1	Anisole	rt/1	 **1**	84
2	1,2-$(MeO)_2$-Benzene	rt/1	 **2**	94
3	1,3,5-$(MeO)_3$-Benzene	rt/0.25	 **3**	71
4	1-(MeO)-Naphthalene	rt/1	 **4**	88
5	2-(MeO)-Toluene	rt/1	 **5**	94
6	4-(MeO)-Toluene	rt/1	 **6**	90
7	1,2-Me_2-Benzene	50/3	 **7**	73
8	1,3-Me_2-Benzene	50/3	 **8**	72
9	1,2,3-Me_3-Benzene	50/3	 **9**	78
10	1-Me-Naphthalene	50/3	 **10**	97

[a] Reaction conditions: arene (8 mmol), benzaldehyde (2 mmol), acetyl bromide (4 mmol), $ZnBr_2/SiO_2$ (0.67 g, 0.8 mmol of $ZnBr_2$ on SiO_2), benzene (15 ml).
[b] Isolated yield.

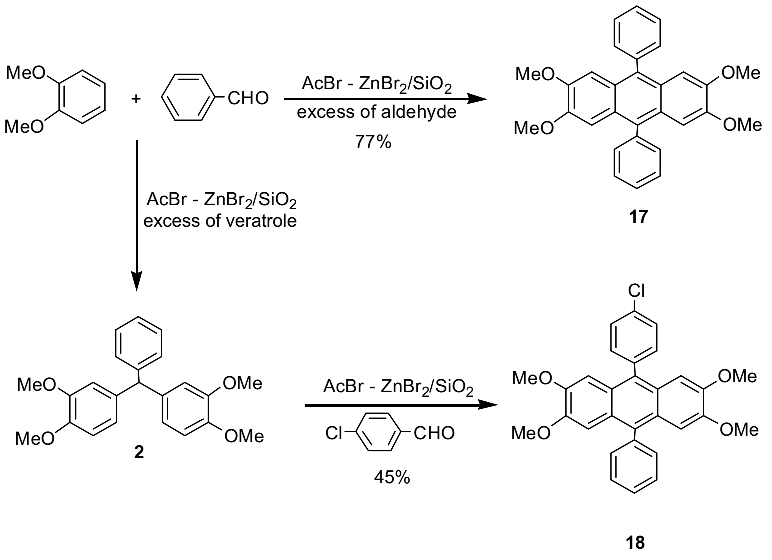
Table 2
Reaction of veratrole (ArH) with various aldehydes leading to triarylmethanes[a]

Entry	Aldehyde (ArH)	Product	Yield[b] (%)
1	Benzaldehyde	 **2**	94
2	4-Cl-Benzaldehyde	 **11**	97
3	4-NO$_2$-Benzaldehyde	 **12**	80
4	4-CHO-Benzaldehyde	 **13**	82
5	4-Me-Benzaldehyde	 **14**	81
6	4-MeO-Benzaldehyde	 **15**	Trace
7	1-Naphthyl-aldehyde	 **16**	89

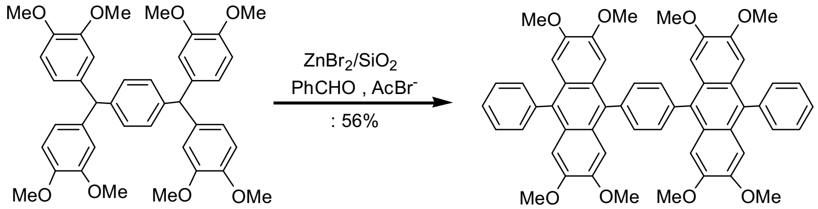
[a] Reaction conditions: veratrole (8 mmol), aldehyde (2 mmol), acetyl bromide (4 mmol), ZnBr$_2$/SiO$_2$ (0.67 g, 0.8 mmol of ZnBr$_2$ on SiO$_2$), benzene (15 ml), room temperature 1 h.

[b] Isolated yield.

Polymethylbenzene such as *o*- and *m*-xylene and 1,2,3-trimethylbenzene required a slightly elevated temperature (50 °C) to condense effectively with benzaldehyde (entries 7–9). 1,3,5-Trimethylbenzene and 1,2,4,5-tetramethylbenzene did not afford the corresponding triarylmethane, and the diarylmethanols were obtained.[13] Toluene did not react under the same conditions, but 1-methylnaphthalene reacted with benzaldehyde at 50 °C to give the triarylmethane **10** in 97% yield (entry 10). Heteroarenes such as 2-methylthiophene and furane failed to give the desired triheteroarylmethane under similar conditions. Next, we tested the generality of the present reaction with veratrole varying the aldehyde partner (Table 2). Reactions were facile with both aromatic aldehydes having an electron-withdrawing and an electron-donating substituent on the aromatic ring. The yield of the product from the reaction with 4-nitrobenzaldehyde was the same as that from the reaction with 4-methylbenzaldehyde (entries 3 and 5). In contrast to these results, 4-methoxybenzaldehyde failed to give the desired triarylmethane. In the literature, benzaldehyde reacts with veratrole in the presence of sulfuric acid to give triarylmethane **2**, but 1-naphthaldehyde does not yield the desired triarylmethane and only starting material is recovered from the reaction mixture.[14] In contrast, reaction of 1-naphthaldehyde with AcBr and veratrole in the presence of ZnBr$_2$/SiO$_2$ took place at room temperature to give **16** in 89% yield (entry 7). For terephthaldehyde having two aldehyde moieties in the same substrate, the desired product was obtained in high yields when veratrole was used in excess (6 equiv with respect to aldehyde) (entry 4). It has been known that acetyl halide combines with aldehydes to afford the adduct (α-halo ester) in the presence of Lewis acid.[15] Therefore, it can be assumed that α-halo ester is an intermediate in the reaction of arenes with AcBr and aldehydes in the presence of ZnBr$_2$/SiO$_2$, leading to triarylmethanes. To test this, α-bromobenzyl acetate was allowed to react with anisole in the presence of ZnBr$_2$/SiO$_2$ at room temperature. As we hoped, the main product was triarylmethane **1** (49% yield). The reaction of benzaldehyde with acetyl bromide in the absence of anisole under the same conditions afforded α-bromobenzyl acetate in 80% yield. Even though we are away from realizing the exact mechanism for the present reaction, α-halo ester may be



Scheme 1.

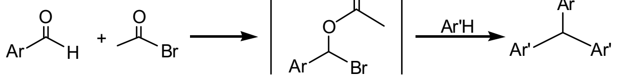


13

19

Scheme 2.

considered as an intermediate in the reaction. Aromatic aldehyde reacts with AcBr at first and then α-bromoaryl acetate yielded reacts with an arene to give a triarylmethane.



When the ratio of arene:aldehyde is changed from 4:1 to 1:3, disubstituted anthracenes were obtained in good yields. For example, the reaction of veratrole (1 equiv) with benzaldehyde (3 equiv) and AcBr (4 equiv) in benzene was carried out in the presence of ZnBr$_2$/SiO$_2$ at room temperature for 4 h to give anthracene **17** in 77% yield. It can be assumed that diveratrylphenylmethane **2** is an intermediate in the reaction with excess benzaldehyde, leading to **17**. To test this, the reaction of **2** with 4-chlorobenzaldehyde (ratio 1:1) was carried out under similar conditions. As we hope, the unsymmetrically substituted anthracene **18** was obtained in 45% yield (Scheme 1).

Furthermore, tetrakis(veratrole)adduct **13** was reacted with benzaldehyde to afford a molecule having two anthracene moieties **19** in 56% yield (Scheme 2).[16] In summary, we have developed a facile method for the synthesis of triarylmethanes and 9,10-diarylanthracenes from the reaction of electron-rich arenes with aromatic aldehydes and acetyl bromide using ZnBr$_2$/SiO$_2$ under mild conditions. We believe that the present procedure provides a useful method for the synthesis of triarylmethanes and 9,10-diarylanthracenes, which are very important compounds in pharmaceutical but also in material fields.

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11. Silica gel-supported zinc bromide was prepared as follows. Silica gel (Wakogel C-200, 36.5 g) was added to a solution of zinc bromide (60 mmol, 13.5 g) in water (100 ml), and the mixture was stirred at room temperature for 0.5 h. The water was removed by a rotary evaporation and the resulting reagent was then dried in vacuo (15 mmHg) at 150 °C for 10 h. 1.2 mmol of ZnBr$_2$ is supported on 1 g of ZnBr$_2$/SiO$_2$.
12. *General procedure for the synthesis of triarylmethanes*: A solution of acetyl bromide (4 mmol) in benzene (5 ml) was added dropwise to a mixture of aromatic aldehyde (2 mmol), an arene (8 mmol) and ZnBr$_2$/SiO$_2$ (0.5 g) in benzene (10 ml) at room temperature. After addition, the suspension was stirred for 1 h at room temperature. The reaction was quenched with water (20 ml) and silica gel was removed by filtration. The organic layer was separated and washed with aqueous solution of NaHCO$_3$ and water. After evaporation of the solvent, the crude product was purified chromatographically. Compound **11** (97%); mp 193–194 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H (ppm) 2.66 (6H, s, 2CH$_3$), 6.78 (2H, d, $J = 7.1$ Hz, H-Ar), 6.80 (1H, s, CH), 7.13 (2H, d, $J = 7.1$ Hz, H-Ar), 7.15–7.33 (5H, m, H-Ar), 7.36 (2H, t, $J = 7.0$ Hz, H-Ar), 7.47 (2H, t, $J = 7.1$ Hz, H-Ar), 7.98 (2H, d, $J = 8.0$ Hz, H-Ar), 8.30 (2H, d, $J = 8.3$ Hz, H-Ar). HRMS (EI): calcd for $C_{29}H_{24}$ M$^+$ 372.1878, found 372.1872.
13. 1,3,5-Trimethylbenzene gave 2,4,6-trimethyl-α-phenylbenzenemethanol in 78% yield and 1,2,4,5-tetramethylbenzene gave 2,3,5,6-tetramethyl-α-phenyl-benzenemethanol in 71% yield.
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16. Compound **19**: mp 302–304 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ_H (ppm) 3.77 (12H, s, 4CH$_3$), 3.79 (12H, s, 4CH$_3$), 6.89 (4H, s, H-Ar), 7.08 (4H, s, H-Ar), 7.52–7.67 (10H, m, H-Ar), 7.78 (4H, s, H-Ar). HRMS (TOF-CI): calcd for $C_{54}H_{47}O_8$ [M+H]$^+$ 823.3270, found 823.3267.