Efficient Conversion of Acetophenones into 1,3,5-Triarylbenzenes Catalyzed by Bismuth(III) Trifluoromethanesulfonate Tetrahydrate

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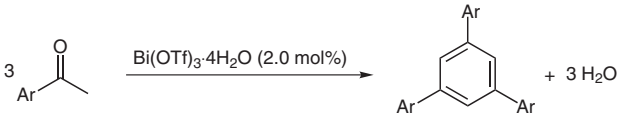
Abstract: Bismuth(III) trifluoromethanesulfonate tetrahydrate is found to efficiently catalyze the cyclotrimerization of acetophenones into 1,3,5-triarylbenzenes in good yields.

Key words: bismuth(III) trifluoromethanesulfonate, catalysis, ketones, Lewis acids, 1,3,5-triarylbenzenes

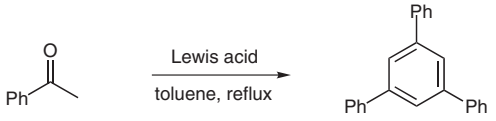
1,3,5-Triarylbenzenes are useful compounds in the fields of electrode and electroluminescent devices[1] and resist materials[2] or in the chemistry of conducting polymers.[3] Their preparation via triple condensation of aryl methyl ketones has been regarded as a useful general method and has been extensively studied.[4] Acid catalysts such as dry HCl,[4,5] PTSA/$SnCl_4$,[6] $SiCl_4$,[7] $TiCl_4$[8], $TiCl_3$(OTf),[9] and solid acid catalysts[10] are widely used for this transformation. However, these methods often involve the use of large amounts of catalysts which are expensive, moisture sensitive, toxic, and produce unsatisfactory yields, especially with *ortho*-substituted acetophenones.[5,10b] Therefore, the introduction of a new and efficient method for this transformation is still in demand. Recently, bismuth(III) trifluoromethanesulfonate has attracted the attention of synthetic organic chemists because it is relatively nontoxic, readily available at low cost, and is fairly insensitive to small amounts of water. Owing to its unique catalytic properties, bismuth(III) trifluoromethanesulfonate has been extensively used for a plethora of organic transformations.[11] However, there have been no reports on the use of bismuth(III) trifluoromethanesulfonate for the cyclotrimerization of acetophenones into 1,3,5-triarylbenzenes. Here, we wish to report that bismuth(III) trifluoromethanesulfonate tetrahydrate (2.0 mol%) is a very efficient catalyst for the cyclotrimerization of acetophenones into 1,3,5-triarylbenzenes (Scheme 1).

First, the cyclotrimerization of acetophenone was carried out in the presence of various Lewis acids (2.0 mol%) in toluene at refluxing temperature for five hours (Table 1).



Scheme 1

Table 1 Cyclotrimerization of Acetophenone in the Presence of Various Lewis Acids[a]



Entry	Lewis acid	Yield (%)[b]
1	Amberlyst 15[c]	3
2	TfOH	55
3	$AlCl_3$	0
4	$SiCl_4$	0
5	Me_3SiOTf	43
6	$Sc(OTf)_3$	0
7	$TiCl_4$	0
8	$TiCl_3$(OTf)[d]	14
9	$FeCl_3$	0
10	$ZrCl_4$	0
11	$InBr_3$	0
12	$SnCl_4$	0
13	$Bi(OTf)_3·4H_2O$	85 (80)
14[e]	$Bi(OTf)_3·4H_2O$	(74)
15	$Bi(NO_3)_2$	0
16	$Bi_2(SO_4)_3$	0
17	$BiCl_3$	0

[a] Reaction conditions: PhCOMe (6.0 mmol), Lewis acid (0.12 mmol), toluene (3 mL), reflux, 5 h, unless otherwise noted.
[b] Based on GC. Isolated yield is given in the parentheses.
[c] Amberlyst 15 (100 mg) was used.
[d] Prepared in situ from $TiCl_4$ (0.12 mmol) and AgOTf (0.12 mmol).
[e] $Bi(OTf)_3·4H_2O$ (0.024 mmol), 32 h.

After screening various conditions, we found that $Bi(OTf)_3·4H_2O$ is a very effective catalysis for the cyclotrimerization reaction (entry 13).

Among bismuth(III) salts screened, we found $Bi(OTf)_3·4H_2O$ to be effective, while inferior results were obtained with $Bi(NO_3)_3$, $Bi_2(SO_4)_3$, and $BiCl_3$ (entries 15–17). Even with 0.40 mol% of $Bi(OTf)_3·4H_2O$, this trans-

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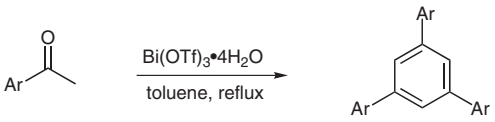
formation proceeded well, but took longer to complete (entry 14).

We next examined the same reaction using various structurally diverse *para*- and *meta*-substituted acetophenones (Table 2). As shown in Table 2, acetophenones carrying either electron-withdrawing or electron-donating groups could be efficiently converted into the corresponding 1,3,5-triarylbenzenes in good yields.

Table 2 Cyclotrimerization of Acetophenones into 1,3,5-Triarylbenzenes Using $Bi(OTf)_3{\cdot}4H_2O$[a]



Entry	Ar	Time (h)	Yield (%)[b]
1	Ph	5	80
2	4-MeC_6H_4	7	82
3	4-$Me_2CHC_6H_4$	4.5	74
4	4-PhC_6H_4	4	90
5	4-FC_6H_4	18	79
6	4-ClC_6H_4	5.5	73
7	4-BrC_6H_4	11	72
8	4-IC_6H_4	4.5	76
9	3-MeC_6H_4	4	78
10	3-ClC_6H_4	13	80

[a] Reaction conditions: ArCOMe (6.0 mmol), $Bi(OTf)_3{\cdot}4H_2O$ (0.12 mmol), toluene (3 mL), reflux.
[b] Isolated yield.

The noteworthy feature of our protocol is that *ortho*-substituted acetophenones, which are difficult to undergo cyclotrimerization by other methods,[5,10b,12] could be easily converted into the corresponding 1,3,5-triarylbenzenes (Scheme 2). For example, treatment of 2-methylacetophenone with $Bi(OTf)_3{\cdot}4H_2O$ (2.0 mol%) at 140 °C for four hours under neat conditions[13] afforded 1-[3,5-bis(2-methylphenyl)phenyl]-2-methylbenzene, which is a key intermediate for the synthesis of truxenone,[7c] in 71% yield.[14]

In a similar manner, 2-chloroacetophenone and 2,5-dimethylacetophenone[15] underwent smooth cyclotrimerization to furnish the desired products in 80% and 70% yields, respectively.

A typical procedure is as follows (Table 1, entry 13): To a mixture of $Bi(OTf)_3{\cdot}4H_2O$[16] (87.4 mg, 0.12 mmol) and toluene (3 mL), acetophenone (721 mg, 6.0 mmol) was added. After the reaction mixture was kept stirring at reflux for five hours, it was quenched by adding saturated $NaHCO_3$ (15 mL). The resulting mixture was extracted with CH_2Cl_2 (2 × 40 mL). The combined extracts were washed with saturated NaCl (10 mL). The organic layer was dried (Na_2SO_4) and concentrated. A GC analysis indicated the formation of 1,3,5-triphenylbenzene in 85% yield relative to *n*-$C_{20}H_{42}$ as an internal standard. The residue was chromatographed on silica gel (20% CH_2Cl_2–hexane) to afford pure 1,3,5-triphenylbenzene (490 mg, 80%).[17]

In conclusion, we have demonstrated an efficient method for cyclotrimerization of acetophenones catalyzed by $Bi(OTf)_3{\cdot}4H_2O$. Further study on $Bi(OTf)_3{\cdot}4H_2O$-catalyzed reaction is currently under way in our laboratory.

References and Notes

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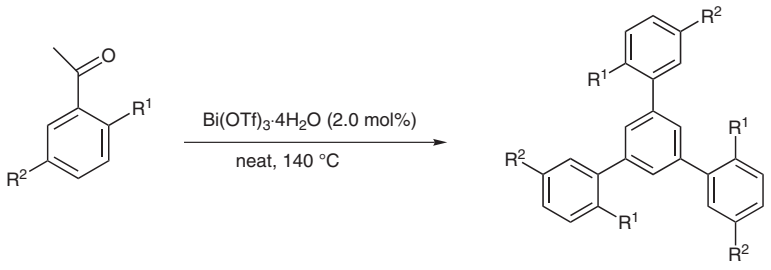

Scheme 2

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(12) To the best of our knowledge, there are only two successful reports[4,7c] on the use of this type of compound in the cyclotrimerization process.
(13) The reaction was very slow in refluxing toluene (12 h, 17%).
(14) Cyclotrimerization of 2-methylacetophenone by the Wirth method [dry HCl(excess), $(EtO)_3CH$ (1.2 equiv), EtOH, r.t., 24 h][4] and the Elmorsy method [$SiCl_4$ (1.0 equiv), EtOH, Δ, 24 h][7c] gave the product in 26% and 32% yields, respectively.
(15) No desired product was obtained by Nafion-H-catalyzed cyclotrimerization of 2,5-dimethylacetophenone.[10b]
(16) Bismuth(III) trifluoromethanesulfonate tetrahydrate was prepared according to the method described in the literature: Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1999**, *40*, 285.
(17) **Selected Physical and Spectroscopic Data**
1,3,5-Triphenylbenzene
Mp 174.1–174.7 °C (Lit.[4] 175–176 °C). MS (EI): *m/z* = 306 $[M]^+$.
1,3,5-Tris(4-methylphenyl)benzene
Mp 175.7–176.9 °C (Lit.[5] 178 °C). MS (EI): *m/z* = 348 $[M]^+$.
1,3,5-Tris[4-(methylethyl)phenyl]benzene
Mp 167.5–168.1 °C (Lit.[5] 166 °C). MS (EI): *m/z* = 432 $[M]^+$.
1,3,5-Tris(4-phenylphenyl)benzene
Mp 236.2–238.0 °C (Lit.[4] 241 °C). MS (EI): *m/z* = 534 $[M]^+$.
1,3,5-Tris(4-fluorophenyl)benzene
Mp 236.5–238.0 °C (Lit.[5] 238 °C). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.17 (t-like, *J* = 8.6 Hz, 6 H), 7.61–7.65 (m, 6 H), 7.66 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 115.8 (d, *J* = 21.6 Hz), 124.8, 128.9 (d, *J* = 8.3 Hz), 137.0 (d, *J* = 4.1 Hz), 141.5, 162.7 (d, *J* = 245.8 Hz). MS (EI): *m/z* = 360 $[M]^+$.
1,3,5-Tris(4-chlorophenyl)benzene
Mp 244.1–244.9 °C (Lit.[5] 246 °C). MS (EI): *m/z* = 408 $[M]^+$.
1,3,5-Tris(4-bromophenyl)benzene
Mp 260.2–260.9 °C (Lit.[5] 262 °C). MS (EI): *m/z* 539 $[M]^+$.
1,3,5-Tris(4-iodophenyl)benzene
Mp 264.6–265.9 °C (Lit.[5] 265 °C). MS (EI): *m/z* = 683 $[M]^+$.
1,3,5-Tris(3-methylphenyl)benzene
Mp 116.8–118.1 °C (Lit.[4] 118 °C).^1H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 9 H), 7.21 (d, *J* = 7.7 Hz, 3 H), 7.37 (t, *J* = 7.7 Hz, 3 H), 7.50 (d, *J* = 7.7 Hz, 3 H), 7.51 (s, 3 H), 7.75 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 124.4, 125.1, 128.1, 128.2, 128.7, 138.4, 141.2, 142.3. MS (EI): *m/z* = 348 $[M]^+$.
1,3,5-Tris(3-chlorophenyl)benzene
Mp 172.4–173.0 °C (Lit.[5] 171 °C). MS (EI): *m/z* = 408 $[M]^+$.
1,3,5-Tris(2-methylphenyl)benzene
Mp 135.6–135.8 °C (Lit.[4] 134–135 °C). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.37 (s, 9 H), 7.22–7.34 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6, 125.8, 127.3, 128.5, 129.9, 130.4, 135.4, 141.5, 141.7. MS (EI): *m/z* = 348 $[M]^+$.
1,3,5-Tris(2-chlorophenyl)benzene
Mp 165.1–165.5 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.36 (m, 6 H), 7.45–7.52 (m, 6 H), 7.58 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 126.9, 128.7, 129.8, 130.1, 131.6, 132.6, 138.9, 139.9. MS (EI): *m/z* = 408 $[M]^+$. HRMS (EI): *m/z* calcd for $C_{24}H_{15}Cl_3$: 408.0242; found: 408.0236.
1,3,5-Tris(2,5-dimethylphenyl)benzene
Mp 148.3–149.4 °C (Lit.[4] 149 °C). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.32 (s, 9 H), 2.35 (s, 9 H), 7.08 (d, *J* = 8.0 Hz, 3 H), 7.15 (s, 3 H), 7.17 (d, *J* = 8.0 Hz, 3 H), 7.26 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2, 20.9, 127.9, 128.4, 130.3, 130.6, 132.2, 135.2, 141.5, 141.6. MS (EI): *m/z* = 390 $[M]^+$.