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# Bi(OTf)$_3$-catalyzed acylation of *p*-quinones: a facile synthesis of acylated hydroquinones

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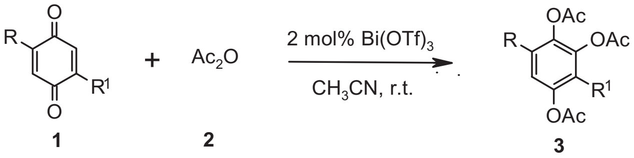
**Abstract**—*p*-Quinones undergo smooth acylation with acetic anhydride in the presence of 2 mol% of bismuth triflate under mild conditions to afford the corresponding 1,4-diacylated-2-acetoxylated hydroquinones in excellent yields with high selectivity.

Hydroxyhydroquinones are widely distributed in nature and are known to possess a broad spectrum of biological activities.[1] Many functionalized hydroxyquinones are extensively used as anti-oxidants, in the photo-industry and as polymeric materials.[2,3] In addition, many quinones derived from aromatic compounds are used as dienophiles in the Diels–Alder reaction.[4] Thus the synthesis of hydroxyquinones is of some importance. The Thiele–Winter acetoxylation is one of the most simple and straightforward approaches for the synthesis of the triacetoxyaromatic precursors of hydroxyquinones.[5a] The method involves the reaction of quinones with acetic anhydride and is generally catalyzed by sulfuric acid.[5b] The use of sulfuric acid results in the formation of tars in some cases, due to its strong acidity and oxidizing character. Zinc chloride has been reported as a milder catalyst[5c] but generally chloroquinones are formed as by-products.[5a] Subsequently, boron trifluoride, perchloric acid and triflic acid have been found to give higher yields than sulfuric acid.[6–8] However, quinones bearing electron-donating groups failed to give the desired triacetates with boron trifluoride or sulfuric acid as the catalyst.[7c]

Lanthanide triflates are unique Lewis acids that are currently of interest.[9] The high catalytic activity, low toxicity, moisture and air tolerance, and their recyclability, make the use of lanthanide triflates attractive alternatives to conventional Lewis acids.[10] However, lanthanide triflates are rather expensive and their use in large-scale synthesis is limited. Therefore, cheaper and more efficient catalysts are desirable. Bismuth triflate has evolved as a remarkable Lewis acid catalyst for effecting various organic transformations.[11] Compared to lanthanide triflates, bismuth triflate is cheap and is easy to prepare even on a multi-gram scale, from commercially available bismuth oxide and triflic acid.[12]

We wish to report a procedure for the synthesis of 1,4-diacylated-2-acetoxylated hydroquinones using a catalytic amount of Bi(OTf)$_3$ under mild conditions. Thus, treatment of *p*-benzoquinone **1** ($R = R' = H$) with acetic anhydride **2** in the presence of 2 mol% of Bi(OTf)$_3$ resulted in the formation of 1,2,4-triacetoxybenzene **3a** ($R = R' = H$) in 91% yield (Scheme 1).

The reaction was complete in a short time (45 min). Substituted benzoquinones, such as 2-methyl-, 2-ethoxy-, 2-methoxy-, 2,3-dimethyl-, 2,5-dimethyl-, 2,6-dimethyl-, and 2,5-dichloro-derivatives also reacted rapidly with acetic anhydride to afford the corresponding tri-acetoxybenzenes (Table 1, entries b–h) in moderate to excellent yields. With mono-substituted quinones such



**Scheme 1.**

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*Keywords*: *p*-Quinones; Acid anhydride; Thiele–Winter reaction; Bismuth triflate.

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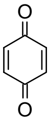
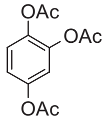
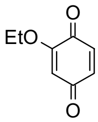
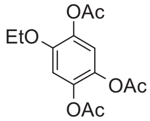
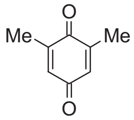
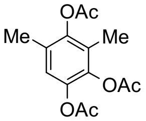
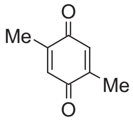
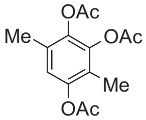
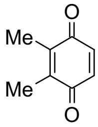
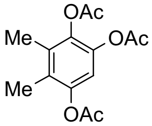
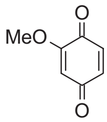
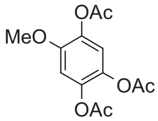
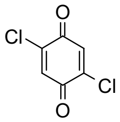
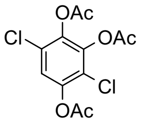
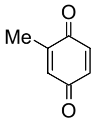
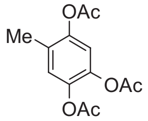
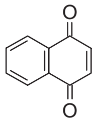
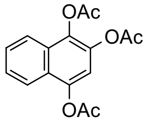
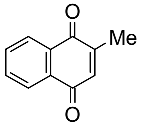
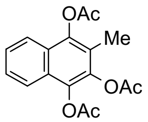
**Table 1.** Bismuth(III) triflate catalyzed acylation of *p*-quinones with acetic anhydride

| Entry | Quinone **1** | Product[a] **3** | Reaction time (min) | Yield (%)[b] |
|---|---|---|---|---|
| a |  |  | 45 | 91 |
| b |  |  | 50 | 65 |
| c |  |  | 55 | 86 |
| d |  |  | 60 | 82 |
| e |  |  | 55 | 85 |
| f |  |  | 70 | 68 |
| g |  |  | 60 | 70 |
| h |  |  | 70 | 79 |
| i |  |  | 45 | 84 |
| j |  |  | 50 | 75 |

[a] All products were characterized by $^1$H NMR, IR, and mass spectroscopy.

[b] Isolated and unoptimized yields.

as 2-methyl-1,4-benzoquinone, 2-ethoxy- or 2-methoxy-1,4-benzoquinone, the addition occurred selectively at the 5-position (Table 1, entries b, f, h) to give 1,2,4-triacetoxy derivatives. 1,4-Naphthoquinone and 2-methylnaphthoquinone (menadione) also afforded triacetoxy derivatives under these conditions (Table 1, entries i and j), even though, 2-methylnaphthoquinone fails to produce a triacetate under the literature conditions (even in the presence of sulfuric acid or boron trifluoride as the catalyst).[5a] The triacetate derived from menadione is a precursor of phthiocol, an antibiotic isolated from *Mycobacterium tuberculosis*.[13] In all cases, the reactions proceeded rapidly at room temperature with high efficiency. As a solvent, acetonitrile appeared to give the best results. The products were characterized by $^1$H NMR, IR, and mass spectroscopic data and also by comparison with authentic samples.[5a] This method is clean and free from the chlorinated side products which are normally observed under zinc chloride catalysis.[5c] The method works well with both electron-donating as well as electron-deficient benzoquinones to give the corresponding triacetates. However, most other methods which fail to produce a triacetate with 2-methylnaphthoquinone are also reported to give lower conversions with methoxy- or ethoxy-substituted quinines as found here. Among the metal triflates such as Cu(OTf)$_2$, Yb(OTf)$_3$, In(OTf)$_3$, and Ce(OTf)$_3$ studied for this transformation, bismuth(III) triflate was found to be the more effective in terms of conversion and reaction rates. However, similar results were also obtained using 5 mol% of scandium(III) triflate.[13]

In conclusion, we describe a simple and highly efficient protocol for the preparation of 1,2,4-triacetylated hydroquinones via Thiele–Winter reaction using bismuth(III) triflate as a novel catalyst.

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13. *General procedure:* A mixture of *p*-quinone **1** (2 mmol), Bi(OTf)$_3$ (0.05 mmol) and acetic anhydride (8 mmol) in acetonitrile (10 mL) was stirred at room temperature for the specified time (see Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate (2 × 10 mL). Evaporation of the solvent followed by purification on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 0.5/9.5) afforded pure product. Spectral data for selected products: **3d**: *2,5-Dimethyl-3,4-di-acetoxyphenyl acetate* (see Table 1): solid, mp 96–98 °C. IR (KBr): $\nu$ 2929, 1763, 1439, 1377, 1194, 1079, 1015, 923, 823 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 1.95 (s, 3H), 2.20 (s, 3H), 2.30 (s, 9H), 6.80 (s, 1H). $^{13}$C NMR (75 MHz, proton decoupled): $\delta$ 168.6, 167.7, 167.5, 146.7, 141.8, 139.1, 129.4, 122.4, 121.3, 20.6, 20.1, 20.1, 15.9, 10.0. FAB MS: $m/z$ (%): 280 M$^+$ (30), 260 (25), 238 (35), 196 (60), 154 (100), 121 (20), 107 (10), 75 (40). HRMS calcd for $C_{14}H_{16}O_6$: 280.0946. Found: 280.0909. **3f**: *2-Methoxy-4,5-di-acetoxyphenyl acetate* (see Table 1): solid, mp 128–130 °C. IR (KBr): $\nu$ 2940, 1771, 1618, 1505, 1371, 1198, 1159, 1014, 919 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.25–2.35 (m, 9H), 3.90 (s, 3H), 6.80 (s, 1H), 6.92 (s, 1H). $^{13}$C NMR (75 MHz, proton decoupled): $\delta$ 166.6, 166.4, 166.3, 147.6, 138.5, 135.4, 133.3, 116.3, 106.3, 54.9, 19.3, 18.8, 18.5. EIMS: $m/z$ (%): 282 M$^+$ (10), 241 (30), 199 (45), 156 (100), 142 (25), 43 (65). HRMS calcd for $C_{13}H_{14}O_7$: 282.0739. Found: 282.0783. **3h**: *2-Methyl-4,5-di-acetoxyphenyl acetate*: solid, mp 102–104 °C. IR (KBr): $\nu$ 2930, 1769, 1509, 1371, 1219, 772 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.10 (s, 3H), 2.15–2.20 (m, 9H), 6.90 (s, 1H), 7.0 (s, 1H). $^{13}$C NMR (50 MHz, proton decoupled): $\delta$ 168.6, 167.9, 167.7, 147.7, 142.6, 138.5, 128.4, 120.8, 117.1, 20.8, 20.5, 20.4, 15.7. FAB MS: $m/z$ (%): 266 M$^+$ (15), 224 (50), 182 (40), 140 (100), 43 (60). HRMS calcd for $C_{13}H_{14}O_6$: 266.0790. Found: 266.0756. **3i**: *1,4-Di(methylcarbonyloxy)-2-naphthyl acetate*: solid, mp 91–92 °C. IR (KBr): $\nu$ 2924, 1775, 1618, 1375, 1097, 915, 801 cm$^{-1}$ $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.30 (s, 9H), 7.05–7.25 (m, 5H). $^{13}$C NMR (75 MHz, proton decoupled): $\delta$ 170.3, 169.5, 169.3, 146.1, 140.2, 136.5, 129.7, 129.2, 128.2, 127.2, 123.4, 123.2, 116.2, 22.5, 22.3, 21.9. EIMS: $m/z$ (%): 302 M$^+$ (10), 210 (15), 168 (30), 126 (85), 110 (40), 43 (100). HRMS calcd for $C_{16}H_{14}O_6$: 302.0791. Found: 302.0762.