Iodobenzene Dicarboxylates as Transferrable Oxygen Sources: Synthesis of α -Oxygenated Ketones from Terminal Aryl Alkynes

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A facile and efficient method for preparation of α -oxygenated ketones has been developed via the reaction of terminal aryl alkynes with various iodobenzene dicarboxylates. When bis(trifluoroacetoxy)iodobenzene (PIFA) was used, α -hydroxy ketones were obtained in high to excellent yields. The hypervalent iodine(III) reagents can function as an electrophile, transferrable *O*-nucleophile, and an excellent leaving group. The protocol represents a direct, atom-efficient and metal-free conversion of alkynes into α -oxygenated ketones under mild conditions.

Keywords iodobenzene dicarboxylates, transferrable oxygen sources, α -oxygenated ketones

Introduction

α -Oxygenated ketones, including α -hydroxy ketones, are common structural motifs in a variety of natural products and represent one class of important intermediates in the synthesis of biologically active compounds and pharmaceuticals. To date, many procedures have been developed to prepare α -oxygenated ketones, such as α -oxygenation of enolates,^[1] epoxidation,^[2] dihydroxylation,^[3] aminoxylation^[4] of preformed enol ethers, enolates and enamines, and reduction of diketones.^[5]

In the past decade, the application of hypervalent iodine(III) reagents in organic synthesis has attracted intense interest due to their intriguing oxidizing properties, low toxicity, mild reactivity, ease of handling and ready availability.^[6] A number of reports have demonstrated the feasibility of iodobenzene diacetate-mediated alkene dioxygenation in the presence or absence of external catalysts^[7,8] and α -oxygenation of ketones.^[9,10] However, the reaction of iodobenzene diacetate with alkynes is less well-documented.^[11] In 2009, Hou and co-workers^[12] reported the reaction of alkynes and iodobenzene diacetate, giving rise to useful α -acetoxy ketones. In this literature, the acetic acid was used as solvent, and the temperature of reaction was at 70 °C. When compared with the Au-catalyzed transformation of alkynes into α -oxygenated ketones,^[13] the method has the distinct advantage of avoiding the utilization of an expensive and toxic transition-metal catalyst. In our research on halogen-mediated organic reactions, we found that this type of reaction can proceed efficiently in the absence of an external acetic acid catalyst and the

reaction temperature can be decreased to room temperature (Scheme 1). The modified conditions developed by our group appear to be much milder and thus more attractive and practical relative to previous research.^[11–13] Through detailed study, we found that various α -acyloxy ketones can be obtained by the reaction of alkynes with a series of iodobenzene dicarboxylates [PhI(OCOR)₂, R = Me, *t*-Bu, and Ph]. Moreover, when bis(trifluoroacetoxy)iodobenzene (PIFA) was used, α -hydroxy ketones were obtained in high to excellent yields. The experimental results demonstrate that PhI(OCOR)₂ itself may serve as a transferrable oxygen source as well as an electrophile and excellent leaving group.^[14]

Scheme 1 Synthesis of α -oxygenated ketones from terminal aryl alkynes.

Experimental

General

All reagents were purchased from Acros, Aldrich

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Chemical Co., Aladdin Industrial and Sinopharm Chemical Reagents Co. They were used without further treatment. The products were purified by column chromatography over silica gel. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Varian 500 MHz and 125 MHz, respectively (TMS as internal standard). IR spectra (KBr) were recorded on a Magna-560 FTIR spectrophotometer in the range of 400–4000 cm^{-1} . Elemental analyses were measured on an E-2400 analyzer (Perkin-Elmer). Mass spectra were recorded on Agilent 1100 LCMsD mass spectrometer.

General procedure for preparation of compounds 2–7 (2a as an example)

To a solution of phenylacetylene **1a** (0.11 mL, 1.0 mmol) in CH_2Cl_2 (2.0 mL) was added $\text{PhI}(\text{OAc})_2$ (384 mg, 1.2 mmol). The mixture was stirred at room temperature for 12 h. The reaction mixture was poured into water and then extracted with CH_2Cl_2 (3×10 mL). The combined organic phase was washed with water (3×10 mL), filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography [silica gel, $V(\text{petroleum ether}) : V(\text{ethyl acetate}) = 3 : 1$] to give **2a** (162 mg, 91%) as a white solid.

Characterization of compounds 2–7

2-Oxo-2-phenylethyl acetate (2a): White solid, m.p. 38–40 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 5.32 (s, 2H), 7.47–7.50 (m, 2H), 7.59–7.62 (m, 1H), 7.90–7.92 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 66.0, 127.7, 128.8, 133.9, 134.1, 170.4, 192.1; IR (KBr) ν : 3415, 2922, 2845, 2353, 1747, 1695, 1383, 1217, 1052, 679 cm^{-1} ; MS m/z (%): 179.2 (M+H, 100). Anal. calcd for $\text{C}_{10}\text{H}_{10}\text{O}_3$: C 67.41, H 5.66; found C 67.68, H 5.63.

2-Oxo-2-(*p*-tolyl)ethyl acetate (2b): White solid, m.p. 81–83 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 2.42 (s, 3H), 5.32 (s, 2H), 7.28 (d, $J=8.5$ Hz, 2H), 7.81 (d, $J=8.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 21.7, 65.9, 127.8, 129.5, 131.7, 144.8, 170.4, 191.7; IR (KBr) ν : 3041, 2954, 1749, 1695, 1604, 1573, 1241, 810 cm^{-1} ; MS m/z (%): 193.1 (M+H, 100). Anal. calcd for $\text{C}_{11}\text{H}_{12}\text{O}_3$: C 68.74, H 6.29; found C 68.55, H 6.27.

2-Oxo-2-(*m*-tolyl)ethyl acetate (2c): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 2.41 (s, 3H), 5.33 (s, 2H), 7.37 (d, $J=7.5$ Hz, 1H), 7.41 (s, 1H), 7.72 (t, $J=7.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 21.2, 66.0, 124.8, 128.1, 128.6, 134.1, 134.6, 138.6, 170.4, 192.2; IR (KBr) ν : 2965, 2928, 1751, 1698, 1612, 1369, 1232, 1087, 959, 806, 781, 605, 560 cm^{-1} ; MS m/z (%): 193.2 (M+H, 100). Anal. calcd for $\text{C}_{11}\text{H}_{12}\text{O}_3$: C 68.74, H 6.29; found C 68.57, H 6.26.

2-(4-(Tert-butyl)phenyl)-2-oxoethyl acetate (2d): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 1.34 (s, 9H), 2.24 (s, 3H), 5.34 (s, 2H), 7.50 (d, $J=8.5$ Hz, 2H), 7.86 (d, $J=8.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ :

20.6, 31.0, 31.1, 35.2, 65.9, 125.8, 127.7, 131.6, 157.7, 170.4, 191.7; IR (KBr) ν : 2972, 2865, 1769, 1692, 1583, 1231, 1084, 987, 841, 734, 639, 581 cm^{-1} ; MS m/z (%): 235.3 (M+H, 100). Anal. calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C 71.77, H 7.74; found C 71.63, H 7.71.

2-(4-Methoxyphenyl)-2-oxoethyl acetate (2e): White solid, m.p. 53–55 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.21 (s, 3H), 3.85 (s, 3H), 5.29 (s, 2H), 6.93 (d, $J=8.5$ Hz, 2H), 7.88 (d, $J=9.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 55.5, 65.7, 114.0, 127.2, 130.0, 164.0, 170.4, 190.6; IR (KBr) ν : 2928, 2837, 1755, 1690, 1587, 1436, 1203, 1169, 1088, 953, 828, 775, 608, 564 cm^{-1} ; MS m/z (%): 209.1 (M+H, 100). Anal. calcd for $\text{C}_{11}\text{H}_{12}\text{O}_4$: C 63.45, H 5.81; found C 63.24, H 5.79.

2-(4-Fluorophenyl)-2-oxoethyl acetate (2f): White solid, m.p. 46–48 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 5.31 (s, 2H), 7.15–7.18 (m, 2H), 7.94–7.97 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 65.8, 116.0, 116.1, 130.4, 130.5, 130.6, 130.6, 165.1, 167.1, 170.3, 190.6; IR (KBr) ν : 3074, 2941, 1746, 1699, 1601, 1509, 1246, 833 cm^{-1} ; MS m/z (%): 197.3 (M+H, 100). Anal. calcd for $\text{C}_{10}\text{H}_9\text{FO}_3$: C 61.22, H 4.62; found C 61.17, H 4.60.

2-(3-Chlorophenyl)-2-oxoethyl acetate (2g): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 5.30 (s, 2H), 7.45 (t, $J=8.0$ Hz, 1H), 7.58–7.59 (m, 1H), 7.78 (d, $J=7.5$ Hz, 1H), 7.89 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.4, 65.8, 125.7, 127.8, 130.1, 133.8, 135.2, 135.5, 170.3, 191.0; IR (KBr) ν : 3038, 2904, 1761, 1735, 1573, 1438, 1372, 1209, 1090, 852, 786, 744, 686, 586 cm^{-1} ; MS m/z (%): 214.0 (M+H, 100). Anal. calcd for $\text{C}_{10}\text{H}_9\text{ClO}_3$: C 56.49, H 4.27; found C 56.25, H 4.25.

2-Oxo-2-(thiophen-2-yl)ethyl acetate (2h): Brown oil; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 5.23 (s, 2H), 7.17 (t, $J=4.5$ Hz, 1H), 7.71 (d, $J=4.5$ Hz, 1H), 7.76 (d, $J=4.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 65.7, 128.2, 131.9, 134.3, 140.3, 170.3, 185.4; IR (KBr) ν : 3012, 1739, 1685, 1483, 1290, 817, 694, 597 cm^{-1} ; MS m/z (%): 185.2 (M+H, 100). Anal. calcd for $\text{C}_8\text{H}_8\text{O}_3\text{S}$: C 52.16, H 4.38; found C 52.43, H 4.39.

2-(4-Ethynylphenyl)-2-oxoethyl acetate (2i): Yellow solid, m.p. 89–91 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.23 (s, 3H), 3.29 (s, 1H), 5.32 (s, 2H), 7.59 (d, $J=9.0$ Hz, 2H), 7.87 (t, $J=4.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 20.5, 65.9, 81.0, 82.5, 127.6, 127.7, 132.5, 133.8, 170.3, 191.4; IR (KBr) ν : 3272, 3070, 2943, 2107, 1744, 1702, 1604, 1557, 1219, 822 cm^{-1} ; MS m/z (%): 203.2 (M+H, 100). Anal. calcd for $\text{C}_{12}\text{H}_{10}\text{O}_3$: C 71.28, H 4.98; found C 71.45, H 4.95.

2-Hydroxy-1-phenylethanone (3a): White solid, m.p. 81–83 °C; ^1H NMR (500 MHz, CDCl_3) δ : 3.53 (s, 1H), 4.89 (s, 2H), 7.51 (t, $J=8.0$ Hz, 2H), 7.86–7.88 (m, 1H), 7.92 (t, $J=4.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 65.4, 127.6, 128.9, 133.2, 134.3, 198.3. IR (KBr) ν : 3417, 3385, 1677, 1432, 1405, 1229, 1095, 971, 761, 689, 617 cm^{-1} ; MS m/z (%): 137.2 (M+H, 100). Anal. calcd for $\text{C}_8\text{H}_8\text{O}_2$: C 70.57, H 5.92; found C 70.32, H 5.94.

2-Hydroxy-1-(*p*-tolyl)ethanone (**3b**): White solid, m.p. 71–73 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.44 (s, 3H), 5.56 (s, 2H), 7.32 (d, $J=8.5$ Hz, 2H), 7.80 (d, $J=8.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 21.8, 65.2, 127.7, 129.6, 145.3, 197.9; IR (KBr) ν : 3439, 2973, 1680, 1612, 1416, 1288, 1165, 965, 754 cm^{-1} ; MS m/z (%): 151.2 (M+H, 100). Anal. calcd for $\text{C}_9\text{H}_{10}\text{O}_2$: C 71.98, H 6.71; found C 71.75, H 6.72.

2-Hydroxy-1-(*m*-tolyl)ethanone (**3c**): White solid, m.p. 57–60 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.43 (s, 3H), 5.56 (s, 2H), 7.41 (t, $J=7.5$ Hz, 1H), 7.46 (d, $J=7.5$ Hz, 1H), 7.69 (t, $J=8.0$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ : 21.2, 65.3, 124.8, 127.3, 128.3, 130.6, 134.4, 135.0, 198.5; IR (KBr) ν : 3450, 2898, 1687, 1293, 1089, 1032, 985, 774, 682 cm^{-1} ; MS m/z (%): 151.1 (M+H, 100). Anal. calcd for $\text{C}_9\text{H}_{10}\text{O}_2$: C 71.98, H 6.71; found C 71.87, H 6.73.

1-(4-(*t*-Butyl)phenyl)-2-hydroxyethanone (**3d**): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 1.35 (s, 9H), 5.57 (s, 2H), 7.53 (d, $J=8.5$ Hz, 2H), 7.85 (d, $J=8.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 30.9, 35.1, 65.2, 125.4, 127.6, 130.0, 157.4, 197.9; IR (KBr) ν : 3420, 2971, 1648, 1505, 1475, 1381, 1225, 937, 853, 796 cm^{-1} ; MS m/z (%): 193.3 (M+H, 100). Anal. calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$: C 74.97, H 8.39; found C 74.75, H 8.36.

2-Hydroxy-1-(4-methoxyphenyl)ethanone (**3e**): White solid, m.p. 64–66 °C; ^1H NMR (500 MHz, CDCl_3) δ : 3.89 (s, 3H), 5.53 (s, 2H), 6.98–7.00 (m, 2H), 7.87–7.89 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 55.5, 67.9, 114.2, 126.2, 130.1, 164.4, 187.1; IR (KBr): 3345, 3027, 2981, 2944, 1688, 1602, 1515, 1468, 1382, 1026, 829 cm^{-1} ; MS m/z (%): 166.1 (M+H, 100). Anal. calcd for $\text{C}_9\text{H}_{10}\text{O}_3$: C 65.05, H 6.07; found C 65.24, H 6.04.

1-(4-Fluorophenyl)-2-hydroxyethanone (**3f**): White solid, m.p. 96–98 °C; ^1H NMR (500 MHz, CDCl_3) δ : 5.55 (s, 2H), 7.21 (t, $J=8.5$ Hz, 2H), 7.93–7.96 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 65.3, 116.3, 129.8, 130.4, 130.5, 167.4, 196.8; IR (KBr) ν : 3391, 3072, 2936, 1685, 1597, 1508, 838 cm^{-1} ; MS m/z (%): 155.1 (M+H, 100). Anal. calcd for $\text{C}_8\text{H}_7\text{FO}_2$: C 62.34, H 4.58; found C 62.13, H 4.54.

1-(3-Chlorophenyl)-2-hydroxyethanone (**3g**): White solid, m.p. 89–91 °C; ^1H NMR (500 MHz, CDCl_3) δ : 5.54 (s, 2H), 7.48 (t, $J=8.0$ Hz, 1H), 7.62–7.64 (m, 1H), 7.77 (d, $J=8.0$ Hz, 1H), 7.87 (t, $J=2.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 59.4, 128.4, 129.6, 129.8, 130.3, 134.1, 134.7, 171.3; IR (KBr) ν : 3432, 3375, 1684, 1607, 1412, 1227, 1164, 1106, 981, 837, 602, 568 cm^{-1} ; MS m/z (%): 172.1 (M+H, 100). Anal. calcd for $\text{C}_8\text{H}_7\text{ClO}_2$: C 56.32, H 4.14; found C 56.02, H 4.11.

2-Hydroxy-1-(thiophen-2-yl)ethanone (**3h**): Brown oil; ^1H NMR (500 MHz, CDCl_3) δ : 4.80 (s, 2H), 7.74 (t, $J=2.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ : 65.4, 128.4, 132.0, 134.5, 139.3, 191.2; IR (KBr) ν : 3432, 3187, 1676, 1533, 1421, 1280, 1072, 943, 864, 720, 589 cm^{-1} ; MS m/z (%): 143.1 (M+H, 100). Anal. calcd for

$\text{C}_6\text{H}_6\text{O}_2\text{S}$: C 50.69, H 4.25; found C 50.37, H 4.29.

1-(4-Ethynylphenyl)-2-hydroxyethanone (**3j**): Yellow solid, m.p. 103–105 °C; ^1H NMR (500 MHz, CDCl_3) δ : 3.32 (s, 1H), 5.56 (s, 2H), 7.62 (d, $J=8.5$ Hz, 2H), 7.86 (d, $J=8.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 68.1, 81.1, 81.5, 127.6, 127.7, 132.6, 132.7, 188.1; IR (KBr) ν : 3432, 3296, 2125, 1686, 1287, 1237, 1125, 953, 817, 565 cm^{-1} ; MS m/z (%): 161.1 (M+H, 100). Anal. calcd for $\text{C}_{10}\text{H}_8\text{O}_2$: C 74.99, H 5.03; found C 74.68, H 5.07.

2-Oxo-2-phenylethyl pivalate (**4**): White solid, m.p. 58–60 °C; ^1H NMR (500 MHz, CDCl_3) δ : 1.31 (s, 9H), 5.32 (s, 2H), 7.48 (t, $J=8.0$ Hz, 2H), 7.59 (t, $J=7.5$ Hz, 1H), 7.90 (t, $J=7.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 27.1, 38.7, 65.8, 127.7, 128.7, 133.7, 134.3, 177.9, 192.4; IR (KBr) ν : 2933, 1737, 1697, 1596, 1576, 1395, 1370, 1149, 688, 669 cm^{-1} ; MS m/z (%): 221.2 (M+H, 100). Anal. calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$: C 70.89, H 7.32; found C 70.63, H 7.35.

2-Oxo-2-phenylethyl benzoate (**5**): White solid, m.p. 91–93 °C; ^1H NMR (500 MHz, CDCl_3) δ : 5.58 (s, 2H), 7.46–7.52 (m, 4H), 7.58–7.62 (m, 2H), 7.97 (t, $J=6.0$ Hz, 2H), 8.14–8.15 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 66.4, 127.8, 128.4, 128.5, 128.8, 129.9, 130.1, 133.3, 133.7, 133.8, 166.0, 192.0; IR (KBr) ν : 3057, 2944, 1718, 1697, 1597, 1581, 1283, 713, 689 cm^{-1} ; MS m/z (%): 241.1 (M+H, 100). Anal. calcd for $\text{C}_{15}\text{H}_{12}\text{O}_3$: C 74.99, H 5.03; found C 74.68, H 5.05.

2-Oxo-2-phenylethane-1,1-diyl bis(4-methylbenzenesulfonate) (**6**): White solid, m.p. 87–89 °C; ^1H NMR (500 MHz, CDCl_3) δ : 2.44 (s, 6H), 6.96 (s, 1H), 7.28 (d, $J=8.5$ Hz, 4H), 7.43–7.47 (m, 2H), 7.59–7.62 (m, 1H), 7.72 (d, $J=8.5$ Hz, 4H), 7.90–7.92 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 195.2, 145.5, 141.4, 136.0, 134.2, 133.1, 130.5, 129.2, 128.6, 103.7, 22.8; IR (KBr) ν : 3047, 2989, 1692, 1608, 1433, 1348, 1274, 987, 802, 699, 576 cm^{-1} ; MS m/z (%): 461.5 (M+H, 100). Anal. calcd for $\text{C}_{22}\text{H}_{20}\text{O}_7\text{S}_2$: C 57.38, H 4.38; found C 57.46, H 4.35.

2-Oxo-2-phenylethyl butyrate (**7**): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ : 0.97–1.01 (m, 3H), 1.69–1.77 (m, 2H), 2.47–2.50 (m, 2H), 5.35 (s, 2H), 7.48 (t, $J=7.5$ Hz, 2H), 7.60 (d, $J=7.5$ Hz, 1H), 7.92 (d, $J=8.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 193.7, 175.1, 135.5, 133.2, 129.2, 128.6, 68.7, 35.8, 19.2, 13.3; IR (KBr) ν : 3047, 2978, 2843, 1740, 1421, 1335, 1244, 1196, 1075, 984, 789, 719 cm^{-1} ; MS m/z (%): 207.0 (M+H, 100). Anal. calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C 69.88, H 6.84; found C 69.95, H 6.81.

Results and Discussion

Initially, the model reaction of phenylacetylene **1a** and $\text{PhI}(\text{OAc})_2$ was examined under various conditions (Table 1). The reactions of **1a** with 1.2 equiv. of $\text{PhI}(\text{OAc})_2$ were performed at room temperature in solvents such as DMF, MeCN, THF and toluene. α -Acetoxy ketone **2a** was obtained in 54%–81% yield

(Table 1, Entries 1–4). Halogenated solvents [CHCl_3 , (dichloroethane) DCE and (dichloromethane) DCM] appear to be more suitable (Table 1, Entries 5–7) and DCM gave the best result (91% yields). Though HOAc was selected as the solvent, the yield exhibited no change (Table 1, Entry 8). Both raising and lowering of the temperature led to decreased yields (Table 1, Entries 9 and 10). 1.0 or 0.8 equiv. of $\text{PhI}(\text{OAc})_2$ was insufficient to drive the reaction to completion (Table 1, Entries 11 and 12). It is noteworthy that the yields exhibit almost no change when dry or wet DCM was used as the solvent.

Table 1 Optimization of the reaction conditions^a

Entry	$\text{PhI}(\text{OAc})_2$ /(equiv.)	Solvent ^b	$T/^\circ\text{C}$	Time/h	Yield ^c /%
1	1.2	DMF	r.t.	12	79
2	1.2	MeCN	r.t.	12	81
3	1.2	THF	r.t.	12	54
4	1.2	PhMe	r.t.	12	57
5	1.2	CHCl_3	r.t.	12	82
6	1.2	DCE	r.t.	12	87
7	1.2	DCM	r.t.	12	91
8	1.2	HOAc	r.t.	12	91
9	1.2	DCM	70	12	85
10	1.2	DCM	0	12	53
11	1.0	DCM	rt	15	81
12	0.8	DCM	rt	15	72

^a Reactions were carried out on a 1.0 mmol scale in 2.0 mL of solvent. ^b No distinct difference in yield was observed when both, dry and wet solvents were used. ^c Isolated yield.

Under the optimized conditions (Table 1, Entry 7), a range of reactions were carried out with various alkynes **1** (1.0 mmol) and $\text{PhI}(\text{OAc})_2$ (1.2 equiv.) in DCM (2.0 mL) (Table 2). The majority of the reactions proceeded efficiently to afford the corresponding α -acetoxy ketones (**2a–2h** and **2j**) in high to excellent yield. The substituents on the terminal arylacetylene may be alkyls (e.g., methyl and *t*-butyl), alkoxy (e.g., methoxy) and halogen atoms (e.g., Cl and F). Heteroaryls such as 2-thienyl worked well, giving acetic acid 2-oxo-2-thiophen-2-yl-ethyl ester (**2h**) in 87% yield, while 2-pyridylacetylene failed, probably due to the strong electron-withdrawing property of the pyridyl group. Bisacetylene can react at one of the triple bonds, affording acetylene-terminated α -acetoxy ketone **2j** in 89% yield. Terminal and internal alkyl alkynes were also investigated with only trace amounts of the target products being observed.

Table 2 Reaction of alkynes with $\text{PhI}(\text{OAc})_2$ ^a

2a , 91%; 90% (5 g scale)	2b , 92%	2c , 91%	2d , 90%
2e , 93%	2f , 88%	2g , 89%	2h , 87%
2i , 0%	2j , 89%	2k , trace	2l , trace

^a Reactions were carried out with **1** (1.0 mmol) and $\text{PhI}(\text{OAc})_2$ (1.2 equiv.) in DCM (2.0 mL) at r.t. for 12 h. The product yields are isolated yields.

To investigate the influence of different ligands on the iodine(III) reagents, the reaction was further examined. Thus, the reaction of alkynes with PIFA was conducted under otherwise identical conditions (Table 3). As a result, instead of the formation of α -trifluoroacetoxy ketones, a series of α -hydroxy ketones **3a–3h** and **3j** were obtained in high to excellent yield (87%–92%). The structure of **3e** was confirmed by single-crystal X-ray diffraction (Figure 1).^[15] A 5 g scale preparation of compounds **2a** and **3a** was readily achieved in excellent yields with simple purification via recrystallization of the crude product from ethanol.

Table 3 Reaction of alkynes with bis(trifluoroacetoxy)iodobenzene^a

3a , 90% 90% (5 g scale)	3b , 92%	3c , 90%	3d , 90%
3e , 92%	3f , 86%	3g , 88%	3h , 87%
3i , 0%	3j , 88%		

^a Reactions were carried out with **1** (1.0 mmol) and PIFA (1.2 equiv.) in DCM (2.0 mL) at r.t. for 12 h. The product yields are isolated yields.

Figure 1 ORTEP drawings of **3e** and **5**.

The reaction was further explored by investigating other hypervalent iodine(III) reagents (Scheme 2).^[16] It was found that the reaction of **1a** with $\text{PhI}(\text{OPiv})_2$ or $\text{PhI}(\text{OBz})_2$ furnished the corresponding α -*t*-butylcarbonyloxy ketone **4** and α -benzyloxy ketone **5** in 86% and 89% yield, respectively [Eq. (1) and (2)].^[17] Interestingly, Koser's reagent [$\text{PhI}(\text{OH})(\text{OTs})$] could also react with **1a** to give α -bistosyloxy ketone **6** in 62% yield [Eq. (3)].^[18,19] The structure of **5** was confirmed by single-crystal X-ray diffraction (Figure 1). Clearly, the reaction was capable of introducing other types of oxygen functionality by simply modulating the ligands on the hypervalent iodine(III) reagent.

Scheme 2 Reaction of alkynes with other hypervalent iodine(III) reagents.

To gain insight into the mechanism, a cross-over experiment was performed (Scheme 3). In the reaction of **1a** and $\text{PhI}(\text{OAc})_2$ (1.2 equiv.), butyric anhydride (1.2 equiv.) was added. As a result, in addition to the formation of **2a** in 51% yield, butyric acid 2-oxo-2-phenyl-ethyl ester (**7**) was also obtained in 43% yield. This provides evidence of the liberation of acetic anhydride in the process, which may further participate in the described transformation. In the control experiments, we found that external HOAc (Table 1, Entry 8) had almost no effect on the reaction yield.

Scheme 3 Control experiment.

On the basis of the results described above, and along with the previous work by Muñiz,^[11,14] Hou,^[12]

and Ochiai,^[20] a plausible mechanism for the conversion of alkynes into α -oxygenated ketones is proposed and depicted in Scheme 4. Reaction of the alkyne with $\text{PhI}(\text{OCOR})_2$ forms the alkynyliodonium intermediate **I**. Then, an intermolecular addition of RCOOH generates vinylidonium intermediate **II**. With the liberation of $(\text{RCO})_2\text{O}$, the iodonium ylide **III** is formed, and further electrophilic addition of $(\text{RCO})_2\text{O}$ to **III** gives intermediate **IV**.^[20] λ^3 -3-iodane **V** is formed via elimination of the acyl cation, followed by protonation. An intramolecular 1,2-acyloxy migration affords the α -acyloxy ketone **2**. Hydrolysis of the α -trifluoroxy ketone delivers the α -hydroxy ketone **3** as the final product. The H^+ source in the **IV** $\rightarrow$ **V** step is supposed to originate from trace amounts of water in the reaction system or directly from the air, considering that the acyl cation liberated is highly moisture-sensitive.

Scheme 4 Proposed mechanism for the formation of α -oxygenated ketones **2** and **3**.

Conclusions

In summary, we have developed an extremely facile and efficient method for synthesis of α -acyloxy ketones and α -hydroxy ketones. Terminal alkyne substrates are functionalized with two C—O bonds using iodobenzene dicarbonate, avoiding the introduction of a transition-metal catalyst. The reaction is practical, highly atom-efficient and uses mild conditions.

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