Efficient and Selective α-Bromination of Carbonyl Compounds with N-Bromosuccinimide under Microwave

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Supporting Information

General Information:
All solvents were purified by standard method. All \textsuperscript{1}H NMR, and \textsuperscript{13}C NMR spectra were recorded using a Bruker AVIII 400 or AVIII 500 spectrometer in CDCl\textsubscript{3} unless otherwise noted. Tetramethylsilane (TMS) served as internal standard (δ = 0) for \textsuperscript{1}H NMR, and CDCl\textsubscript{3} was used as internal standard (δ = 77.0) for \textsuperscript{13}C NMR. Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br =broad). The NMR data were processed using the topspin program version 2.1. The α-bromination of carbonyl compounds with N-bromosuccinimide were performed in a CEM Matthews WC Discover microwave reactor (model no. 908010 DV9068 equipped with programmable pressure and temperature controller). Solvents were freshly dried and degassed according to the purification handbook “Purification of Laboratory Chemicals” before using. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60.
Experimental Section:

**General Procedure for the Microwave Promoted α-Bromination of Carbonyl Compounds with NBS Catalyzed by PTSA**

In a dry 10 mL flask with a Teflon stirring bar were introduced 0.2 mmol of the desired carbonyl compounds, NBS (0.2 mmol, 1 equiv), PTSA (0.02 mmol, 10 mol%). Anhydrous DCM (2 mL) was added, the flask was sealed and the mixture was stirred and irradiated at the corresponding temperature. After 30 min, the reaction mixture was treated with 10 mL of distilled water, extracted with 3*10 mL of CH$_2$Cl$_2$, dried over MgSO$_4$, and purified by flash chromatography to give the corresponding product.

**General Procedure for the α-Bromination of Carbonyl Compounds with NBS Catalyzed by PTSA Under Thermal condition.**

In a dry 10 mL flask with a Teflon stirring bar were introduced 0.2 mmol of the desired carbonyl compounds, NBS (0.2 mmol, 1 equiv), PTSA (0.02 mmol, 10 mol%). Anhydrous DCM (2 mL) was added, the flask was sealed and the mixture was stirred using thermostated oil-bath at the corresponding temperature. After 30 min, the reaction mixture was treated with 10 mL of distilled water, extracted with 3*10 mL of CH$_2$Cl$_2$, dried over MgSO$_4$, and purified by flash chromatography to give the corresponding product.

2-bromo-1-phenylethanone (1b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.46 ( s, 2H ), 7.47-7.51 ( m, 2H ), 7.59-7.72 ( m, 1H ), 7.97-7.99 ( m, 2H ). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.67, 128.51, 128.56, 133.52, 190.93. HRMS (ESI) m/z 197.9680, calc.for [C$_8$H$_7$BrO] 197.9683.

2-bromo-1-(4-nitrophenyl)ethanone (2b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.46 ( s, 2H ), 8.15-8.17 ( m, 2H ), 8.34-8.35 ( m, 2H ). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.67, 128.51, 128.56, 133.52, 190.93. HRMS (ESI) m/z 242.9531, calc.for [C$_8$H$_6$BrNO$_3$] 242.9536.

2-bromo-1-(4-bromophenyl)ethanone (3b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.40 ( s, 2H ), 7.63-7.65 ( m, 2H ), 7.84-7.86 ( m, 2H ). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.01, 128.97, 130.06,131.86, 132.21, 190.07. HRMS (ESI) m/z 275.8785, calc.for [C$_8$H$_6$Br$_2$O] 275.8783.
2-bromo-1-(4-methoxyphenyl)ethanone (4b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.88 (s, 3H), 4.40 (s, 2H), 6.94-6.96 (m, 2H), 7.96-7.97 (m, 2H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.38, 55.21, 113.68, 126.48, 131.00, 163.74, 189.61. HRMS (ESI) m/z 227.9786, calc.for [C$_9$H$_9$BrO$_2$] 227.9790.

2-bromo-1-(4-fluorophenyl)ethanone (5b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.41 (s, 2H), 7.14-7.18 (m, 2H), 8.00-8.03 (m, 2H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.13, 115.65, 115.83, 129.90, 129.92, 131.33, 131.40, 164.74, 166.78, 189.48. $^{19}$F NMR (376MHz, CDCl$_3$) $\delta$ -103.19. HRMS (ESI) m/z 215.9589, calc.for [C$_8$H$_6$BrFO] 215.9589.

2-bromo-1-(4-(trifluoromethyl)phenyl)ethanone (6b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.40 (s, 2H), 7.70-7.72 (m, 2H), 8.04-8.05 (m, 2H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.00, 30.02, 121.91, 121.09, 121.19, 121.9, 129.82, 134.81, 155.92, 191.28. HRMS (ESI) m/z 265.9554, calc.for [C$_9$H$_6$BrF$_3$O] 265.9559.

2-bromo-1-(3-hydroxyphenyl)ethanone (7b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.46 (s, 2H), 6.11 (s, 1H), 7.12-7.14 (m, 1H), 7.35-7.38 (m, 1H), 7.52-7.53 (m, 2H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.83, 114.88, 121.09, 121.19, 129.82, 134.81, 155.92, 191.28. HRMS (ESI) m/z 213.9629, calc.for [C$_8$H$_7$BrO$_2$] 213.9635.

2-bromo-1-(2-bromophenyl)ethanone (8b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.49 (s, 2H), 7.35-7.37 (m, 1H), 7.39-7.42 (m, 1H), 7.46-7.48 (m, 1H), 7.62-7.64 (m, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 33.59, 118.72, 127.3, 129.36, 132.17, 133.34, 138.18, 194.58. HRMS (ESI) m/z 275.8785, calc.for [C$_8$H$_6$Br$_2$O] 275.8788.

2-bromo-1-(2-methoxyphenyl)ethanone (9b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.91 (s, 3H), 4.38 (s, 2H), 6.95-7.02 (m, 2H), 7.47-7.51 (m, 1H), 7.79-7.82 (m, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 37.46, 55.36, 111.20, 120.67, 124.39, 131.16, 134.43, 158.40, 191.92. HRMS (ESI) m/z 227.9786, calc.for [C$_9$H$_9$BrO$_2$] 227.9792.
ethyl 2-bromo-3-oxobutanoate (10b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 1.29-1.32 (t, $J = 7.1$ Hz, 3H), 2.34 (s, 2H), 4.26-4.30 (q, $J = 7.1$ Hz, 2H), 4.75 (s, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 13.53, 26.08, 48.74, 62.85, 164.78, 196.08. HRMS (ESI) m/z 207.9735, calc.for [C$_6$H$_9$BrO$_3$] 207.9738.

ethyl 2-bromo-3-oxo-3-phenylpropanoate (11b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 1.23-1.26 (t, $J = 7.1$ Hz, 3H), 4.26-4.30 (q, $J = 7.1$ Hz, 2H), 5.65 (s, 1H), 7.48-7.51 (m, 2H), 7.61-7.62 (m, 1H), 7.98-8.00 (m, 2H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 13.51, 45.96, 62.97, 128.55, 128.83, 132.93, 133.94, 164.81, 187.75. HRMS (ESI) m/z 269.9892, calc.for [C$_{11}$H$_{11}$BrO$_3$] 269.9896.

2-bromo-3,4-dihydronaphthalen-1(2H)-one (12b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.45-2.54 (m, 2H), 2.90-2.94 (m, 1H), 3.28-3.35 (m, 1H), 4.73 (s, 1H), 7.27-7.29 (m, 1H), 7.34-7.37 (m, 1H), 7.51-7.54 (m, 1H), 8.08-8.10 (m, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 25.72, 31.50, 50.06, 126.75, 128.30, 128.39, 129.51, 133.78, 142.62, 190.26 HRMS (ESI) m/z 223.9837, calc.for [C$_{10}$H$_9$BrO] 223.9843.

2-bromo-2,3-dihydro-1H-inden-1-one (13b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.40-3.44 (dd, $J = 2.8$, 18 Hz, 1H), 3.81-3.86 (dd, $J = 7.6$, 18 Hz, 1H), 4.64-4.66 (m, 1H), 7.41-7.45 (m, 2H), 7.65-7.68 (m, 1H), 7.83-7.84 (m, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 37.59, 43.70, 124.72, 126.07, 127.93, 133.16, 135.63, 150.77, 199.32. HRMS (ESI) m/z 209.9680, calc.for [C$_9$H$_7$BrO] 209.9685.

2-bromo-1-(furan-2-yl)ethanone (14b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.32 (s, 2H), 6.59-6.60 (m, 1H), 7.33-7.34 (m, 1H), 7.64 (s, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.07, 112.91, 119.20, 147.34, 150.33, 180.40. HRMS (ESI) m/z 187.9473, calc.for [C$_6$H$_5$BrO$_2$] 187.9476.

2-bromo-1-(thiophen-2-yl)ethanone (15b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.36 (s, 2H), 7.16-7.18 (m, 1H), 7.72-7.73 (m, 1H), 7.80-7.81 (m, 1H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 30.24, 128.05, 133.19, 134.93, 140.37, 184.07. HRMS (ESI) m/z 203.9244, calc.for [C$_6$H$_5$BrOS] 203.9250.