Benzyltriethylammonium Dichloroiodate / Sodium Bicarbonate Combination as an Inexpensive, Environmentally Friendly and Mild Iodinating Reagent for Anilines.

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Supporting Information.

General: All reactions were performed under an atmosphere of nitrogen unless stated otherwise. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Hexanes and dichloromethane were distilled under nitrogen. Anilines were commercial samples (Aldrich) used without additional purification. Silica gel plates were 250 μm thick, 40 F_{254} grade from EM Science. Silica gel was grade 60 (230-400 mesh) from EM Science. ^{1}H and ^{13}C NMR spectra were obtained at 400 and 100 MHz, respectively. IR assignments have 2 cm^{-1} resolution.

Benzyltriethylammonium dichloroiodate (2) from iodine. Commercial bleach (5.25% NaClO, 100 mL, 80 mmol) was added to iodine (20.32 g, 80 mmol), water (200 mL) and concentrated hydrochloric acid (100 mL) contained in an Erlenmeyer flask sitting in an ice bath at such a rate as to keep the temperature below 20 ºC. Toward the end of the bleach addition, the bleach was added dropwise until the endpoint manifested by the disappearance of the brown coloration of iodine was reached. Then, 10% aqueous NaI was added dropwise to restore the barely visible brown coloration and the resulting orange solution was gradually introduced into a solution of benzyltriethylammonium chloride (36.4 g, 160 mmol) in water (50 mL). The resulting light-yellow precipitate was collected by filtration, washed with water (100 mL, 3X)

and dried *in vacuo* for 12 h to afford light yellow needles (61.84 g, 99% yield): mp 84-86 ºC. (lit.[1] mp 79 ºC). IR (KBr) 3413, 3087, 1578, 1527, 1457, 1350, 1033, 876, 827, 754, 455 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.56 (m, 5 H), 3.95 (q, J=7.3 Hz, 6 H), 1.54 (t, J=7.3 Hz, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.51, 131.51, 130.10, 126.28, 61.57, 53.39, 8.66.

Benzyltriethylammonium dichloroiodate (2) from sodium iodide. Bleach (5.25% NaClO, 480 mL, 350 mmol) was added to sodium iodide (52.50 g, 350 mmol) and concentrated hydrochloric acid (120 mL) contained in an Erlenmeyer flask as described in the previous experiment. The product was isolated as light yellow needles (134.85 g, 99% yield): mp 84-86 ºC. The spectroscopic properties of the salt matched those observed in the previous experiment.

Tetraethylammonium dichloroiodate (3). Commercial bleach (5.25% NaClO, 480 mL, 350 mmol) was added to tetraethylammonium iodide (90.02 g, 350 mmol), dichloromethane (200 mL) and concentrated hydrochloric acid (120 mL) contained in an Erlenmeyer flask sitting in an ice bath at such a rate as to keep the temperature below 20 ºC. Toward the end of the bleach addition it was added dropwise to just destroy the brown coloration of iodine in the organic phase. Then 10% aqueous NaI was added dropwise to restore barely visible brown coloration. The organic layer was separated and the aqueous was extracted with dichloromethane (30 mL, 3X). The combined organic extracts were washed with water (20 mL) twice, dried over Mg_2SO_4, evaporated in vacuo to 100 mL and treated with ether (200 mL) to give the desired product as bright yellow powder (100.3 g, 87% yield): mp 102-104 ºC. IR (KBr) 2983, 1486, 1441, 1392, 1362, 1174, 1071, 1054, 998, 789 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40 (q, J=7.3 Hz, 8 H), 1.46 (tt, J=7.3, 1.9 Hz, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.29, 8.16.

4-Iodoaniline (12). Recovery of the benzyltriethylammonium cation. A solution of benzyltriethylammonium dichloroiodate (97.48 g, 250 mmol) in dichloromethane (100 mL) was added to aniline (23.25 g, 250 mmol), dichloromethane (200 mL), methanol (100 mL) and $NaHCO_3$ (42.0 g, 500 mmol) in a three-neck flask equipped with a magnetic stirring bar and an addition funnel. Immediate and vigorous gas evolution was observed along with a subsequent temperature drop. The reaction mixture was stirred until all aniline was consumed (TLC control with ether/hexanes eluent) and was then poured in water (400 mL). The organic phase was separated, washed with water (50 mL, 3X), dried over $MgSO_4$, and

(1) Vlassa, M., Silberg, I. A., Custelceanu, R., Culea, M. *Synth.Commun.* **1995**, *25*, 3493.

evaporated. The evaporation residue was dissolved in warm hexanes containing 5% ether and filtered to remove the small amount of black oil. Upon cooling, the desired product crystallized as yellowish needles (49.65 g, 91% yield): mp 62-63 ºC (lit.[2] mp 61-62 ºC). Combined aqueous phases were acidified with hydrochloric acid to pH 4 and treated with a dichloroiodate solution prepared from NaI (37.5 g, 250 mmol), concentrated hydrochloric acid (86 mL) and bleach (5.25% NaClO, 340 mL) to give an abundant precipitate of benzyltriethylammonium dichloroiodate that was isolated as described previously (92.33 g, 95% recovery of the benzyltriethylammonium cation).

General procedure for the iodination of substituted anilines. 3-Ethyl-4-iodoaniline (13). A three-neck flask equipped with a magnetic stirring bar and an addition funnel was charged with 3-ethylaniline (2.86 g, 23.60 mmol), dichloromethane (15 mL), methanol (15 mL) and $NaHCO_3$ (3.96 g, 47.2 mmol). The flask was placed in an ice bath, evacuated to induce mild solvent boiling and backfilled with nitrogen 3X. Then a solution of benzyltriethylammonium dichloroiodate (9.20 g, 23.60 mmol) in dichloromethane (15 mL) was added dropwise over a period of 15 min. The reaction mixture was allowed to reach room temperature, stirred for an additional 25 min and worked up as described in the general procedure. After column chromatography on silica (dichloromethane as eluent) the product was isolated as a colorless oil (4.90 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J=8.4 Hz, 1 H), 6.57 (d, J=2.8 Hz, 1 H), 6.26 (dd, J=8.4, 2.8 Hz, 1 H), 3.63 (s, 2 H), 2.62 (q, J=7.5 Hz, 2 H), 1.17 (t, J=7.5 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.19, 146.97, 139.73, 115.65, 115.07, 85.90, 34.11, 14.62.

4-Iodo-2,5-diethylaniline (14). 2,5-Diethylaniline (11.92 g, 80.0 mmol) was treated with benzyltriethylammonium dichloroiodate (31.19 g, 80.0 mmol) in dichloromethane (150 mL) and methanol (60 mL) in the presence of $NaHCO_3$ (13.44 g, 160 mmol) in a three-neck flask equipped with a magnetic stirring bar and an addition funnel as described in the general iodination procedure. The product was isolated as light-yellow needles after crystallization from hexanes (21.81 g, 99%): mp 31-33 ºC. IR (KBr) 3410, 3310, 3214, 2962, 2927, 2868, 2836, 1631, 1486, 1397, 1261, 879 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1 H), 7.25 (s, 1 H), 3.60 (s, 2 H), 2.60 (q, J=7.5 Hz, 2 H), 2.43 (q, J=7.5 Hz, 2 H), 1.23 (t, J=7.5 Hz, 3 H), 1.18 (t, J=7.5 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.82, 144.63, 138.68, 128.41, 115.73,

(2) Veglia, A.V. ; de Rossi, R. H. *J. Org. Chem*. **1988**, *53*; 5281.

86.45, 77.54, 77.23, 76.91, 33.76, 23.46, 14.88, 13.09. HRMS found *m/z* 275.0170, $C_{10}H_{14}NI$ requires 275.0171.

2-Iodo-4,6-dimethylaniline (15). 2,4-Dimethylaniline (0.242 g, 2.00 mmol) was treated with benzyltriethylammonium dichloroiodate (0.780 g, 2.00 mmol) in dichloromethane (4.0 mL) and methanol (2.0 mL) in the presence of $NaHCO_3$ (0.336 g, 4.00 mmol) and contained in a vial equipped with a magnetic stirring bar as described in the general iodination procedure. The product was isolated as pinkish needles (0.369 g, 75%): mp 65-67 ºC (lit.[3] mp 65 ºC). IR (KBr) 3309, 2917, 1622, 1478, 1281, 854, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dq, J=2.0, 0.7 Hz, 1 H), 7.93 (m, 1 H), 2.18 (br s, 3 H), 2.17 (br s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.55, 137.02, 131.60, 129.40, 122.64, 84.95, 20.03, 19.07. HRMS found *m/z* 246.9851, $C_8H_{10}NI$ requires 246.9858.

4-Iodo-2,5-dimethylaniline (16). 2,5-Dimethylaniline (0.242 g, 2.00 mmol) was treated with benzyltriethylammonium dichloroiodate (0.780 g, 2.00 mmol) in dichloromethane (4.0 mL) and methanol (2.0 mL) in the presence of $NaHCO_3$ (0.336 g, 4.00 mmol) in a vial equipped with a magnetic stirring bar as described in the general iodination procedure. The product was isolated as light orange solid (0.494 g, 100%) and purified by recrystallization from ether/hexanes to afford colorless needles (0.469 g, 95%): mp 66-68 ºC (lit.[1] mp 69 ºC). IR (KBr) 3309, 2917, 1622, 1478, 1281, 854, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dq, J=2.0, 0.7 Hz, 1 H), 7.93 (m, 1 H), 2.18 (br s, 3 H), 2.17 (br s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.55, 137.02, 131.60, 129.40, 122.64, 84.95, 20.03, 19.07. HRMS found *m/z* 246.9859, $C_8H_{10}NI$ requires 246.9858.

4-Iodo-3-chloroaniline (17). 3-Chloroaniline (0.255 g, 2.00 mmol) was treated with benzyltriethylammonium dichloroiodate (0.780 g, 2.00 mmol) in dichloromethane (4.0 mL) and methanol (2.0 mL) in the presence of $NaHCO_3$ (0.336 g, 4.00 mmol) in a vial equipped with a magnetic stirring bar as described in the general iodination procedure. The product was isolated as colorless needles (0.499 g, 99%): mp 70-72 ºC (lit.[1] mp 69 ºC). IR (KBr) 3421, 3342, 1620, 1573, 1463, 1410, 1293, 854, 818, 569 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J=8.5 Hz, 1 H), 6.75 (d, J=2.7 Hz, 1 H), 6.27 (dd, J=8.5, 2.7 Hz, 1 H), 3.70 (s, J=8.5, 2.7 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.78, 140.21, 138.63, 115.75, 115.49, 82.55. HRMS found *m/z* 252.9151, C_6H_5ClNI requires 252.9155.

(3) Suzuki,H. et al. *Bull.Chem.Soc.Jpn*. **1965**, *38*, 1590.

***N*-Methyl-4-iodoaniline (18).** *N*-methylaniline (0.214 g, 2.00 mmol) was treated with benzyltriethylammonium dichloroiodate (0.780 g, 2.00 mmol) in dichloromethane (4.0 mL) and methanol (2.0 mL) in the presence of $NaHCO_3$ (0.336 g, 4.00 mmol) in a vial equipped with a magnetic stirring bar as described in the general iodination procedure. The product was isolated as a brown light sensitive oil (0.458 g, 98%). IR (KBr) 3421, 2879, 2810, 1593, 1500, 1317, 1294, 1259, 1182, 811 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, AA' part of AA'XX' pattern, J=8.6, 3.0, 2.2, 0.3 Hz, 2 H), 6.32 (m, XX' part of AA'XX' pattern, J=8.6, 3.0, 2.2, 0.3 Hz, 2 H), 3.67 (s, 3 H), 2.72 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.85, 137.67, 114.65, 77.66, 30.59.

***N*-Phenyl-4-iodoaniline (19).** Diphenylamine (5.07 g, 30.0 mmol) was treated with benzyltriethylammonium dichloroiodate (11.697 g, 30.00 mmol) in dichloromethane (30.0 mL) and methanol (30.0 mL) in the presence of $NaHCO_3$ (5.040 g, 60.0 mmol) in a round bottom flask equipped with a magnetic stirring bar as described in the general iodination procedure. The crude product was isolated as white crystals (8.390 g) containing starting material and 4,4'-diiododiphenylamine (0.67 and 1.30 g, respectively, by the ^1H NMR). Starting material was removed by distillation at 110 ºC (0.20 torr) and the residue was recrystallized from ether/hexanes to afford colorless needles of **19** (5.122 g, 58%): mp 102-104 ºC. IR (KBr) 3398, 1580, 1501, 1481, 1314, 748, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (m, AA' part of AA'XX' pattern, J=8.6, 2.9, 1.9, 0.2 Hz, 2 H), 7.27 (m, AA' part of AA'NN'X pattern, J=8.4, 7.3, 2.4, 1.7, 1.1, 0.4 Hz, 2H), 7.04 (m, NN' part of AA'NN'X pattern, J=8.4, 7.3, 2.4, 1.7, 1.1, 0.4 Hz, 2H), 7.04 (tt, J=7.3, 1.1 Hz, 1H), 6.81 (m, XX' part of AA'XX' pattern, J=8.6, 2.9, 1.9, 0.2 Hz, 2 H), 5.65 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.32, 142.36, 138.26, 129.64, 122.01, 119.46, 118.73, 82.29. HRMS found *m/z* 294.9856, $C_{12}H_{10}NI$ requires 294.9858.