Supporting Information

Bromination from the Macroscopic Level to the Tracer Radiochemical Level: ^{76}Br Radiolabeling of Aromatic Compounds via Electrophilic Substitution

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Synthesis of [^{76}Br]5-bromo-2-furaldehyde ([^{76}Br]3)

Using premixed 2:1 hydrogen peroxide/acetic acid: [^{76}Br]NH_4Br (~10 mCi) was dried in a 5 mL Wheaton V vial at 130 $^{\circ}$C under very gentle N_2 flow. At ambient temperature, acetic acid (20 μL) and a solution of **6** (0.5 mg) in methanol (50 μL) were added, and the solution was vortexed before addition of 2:1 hydrogen peroxide/acetic acid (100 μL, pre-mixed for at least 4 h). Then the reaction mixture was vortexed to homogeneity. Upon completion of the reaction in 30 min (> 80% incorporation according to radio-TLC analysis: silica gel plate, 1:1 ethyl acetate/hexanes, R_f = 0.8), the reaction was quenched by addition of water (2 mL). [^{76}Br]**3** was confirmed by silica radio-TLC and HPLC co-injection with authentic standard **3**. HPLC: Alltech Econosil C18 250×4.6 10μ, 55% acetonitrile, 45% water, 1.5 mL/min, 254 nm, T_R = 4.5 min.

Using peracetic acid: Into a 5 mL Wheaton V vial containing dried [^{76}Br]NH_4Br (~0.9 mCi) were added a solution of **6** (0.3 mg) in methanol (30 μL) and acetic acid (10 μL). The mixture was vortexed to homogeneity, then 1% PAA in 2:1 hydrogen peroxide(35% in water)/acetic acid (60 μL) and the mixture was vortexed again. According to radio-TLC, >90% incorporation of [^{76}Br]bromide was observed within 7 min.

Note: The same procedure for using PAA in 1:1 or 2:1 water/acetic acid mixture. However, organic compounds have better solubility in hydrogen peroxide/acetic acid.

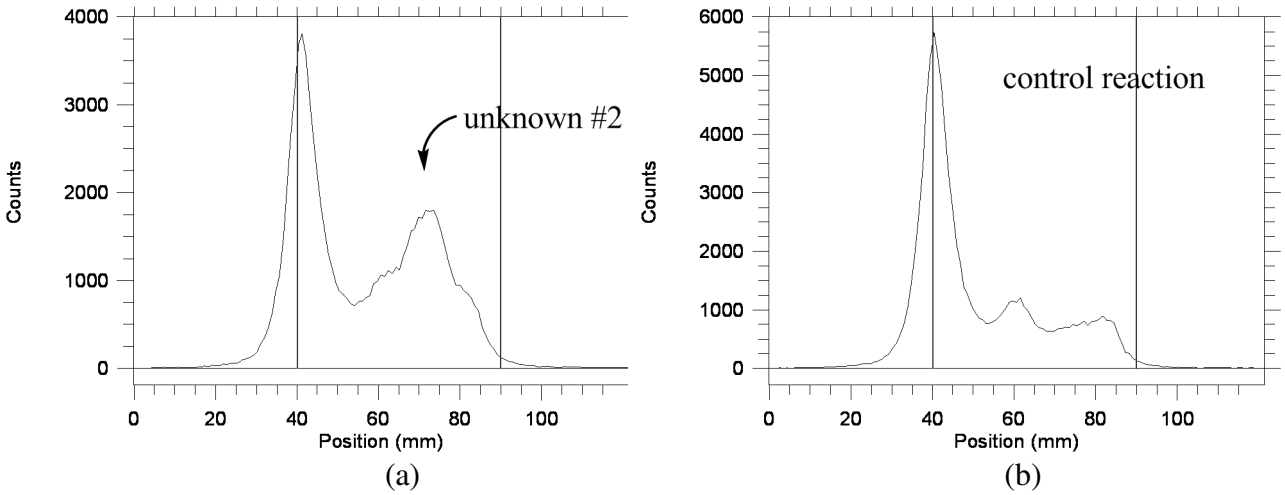


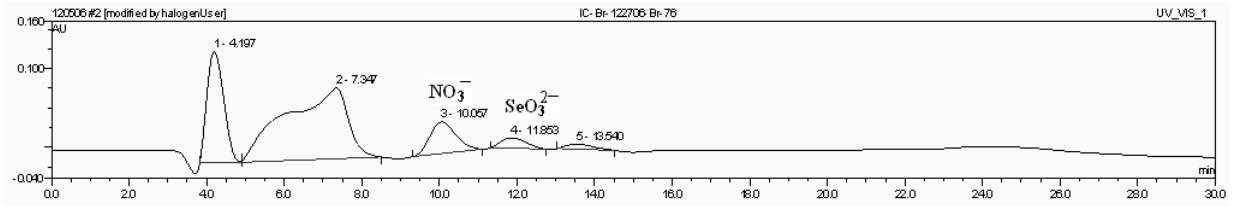
Figure S1. Radio-TLCs of radiobromination of **4** (a) and its control reaction (b) showing the lipophilic byproducts (Silica gel, 4:1 hexanes/ethyl acetate)

Reaction condition:

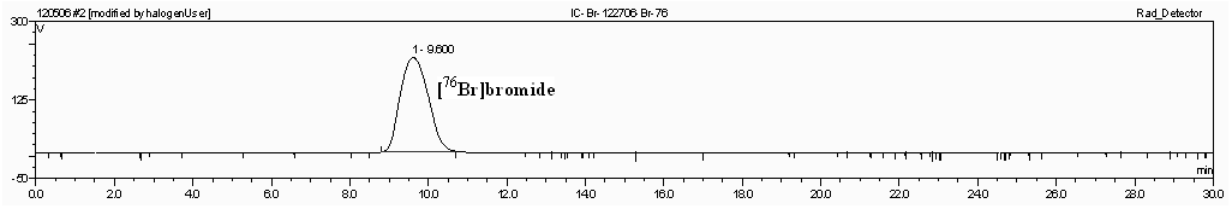
(a) ^{76}Br (produced in water, dried at 130 °C), acetic acid (100 µL), **4** (0.12 mg) in ethanol (20 µL), CAT (50 µL) from a solution of CAT (3.7 mg) in ethanol (2000 µL);

(b) ^{76}Br (produced in water, dried at 130 °C), acetic acid (100 µL), CAT (50 µL) from a solution of CAT (3.7 mg) in ethanol (2000 µL).

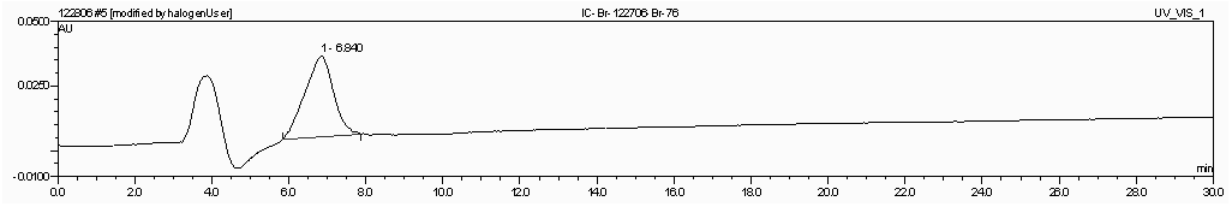
Note: Around 50% of the lipophilic byproducts was from the reaction with **4** (*panel a*), the rest was from the reaction with reactive species in the reaction mixture (*panel b*)



(a)



(b)



(c)

Figure S2. Ion Chromatography of [^{76}Br]bromide extracted in 0.6 N NH_4OH (a) UV trace at 210nm (b) radioactive trace (c) UV trace of 0.6 N NH_4OH only. (UV at 210 nm)

Note: Only [^{76}Br]bromide was observed in the IC, no other radioactive peaks were observed (*panel b*); no NO_3^- was observed in 0.6 N NH_4OH (*panel c*).

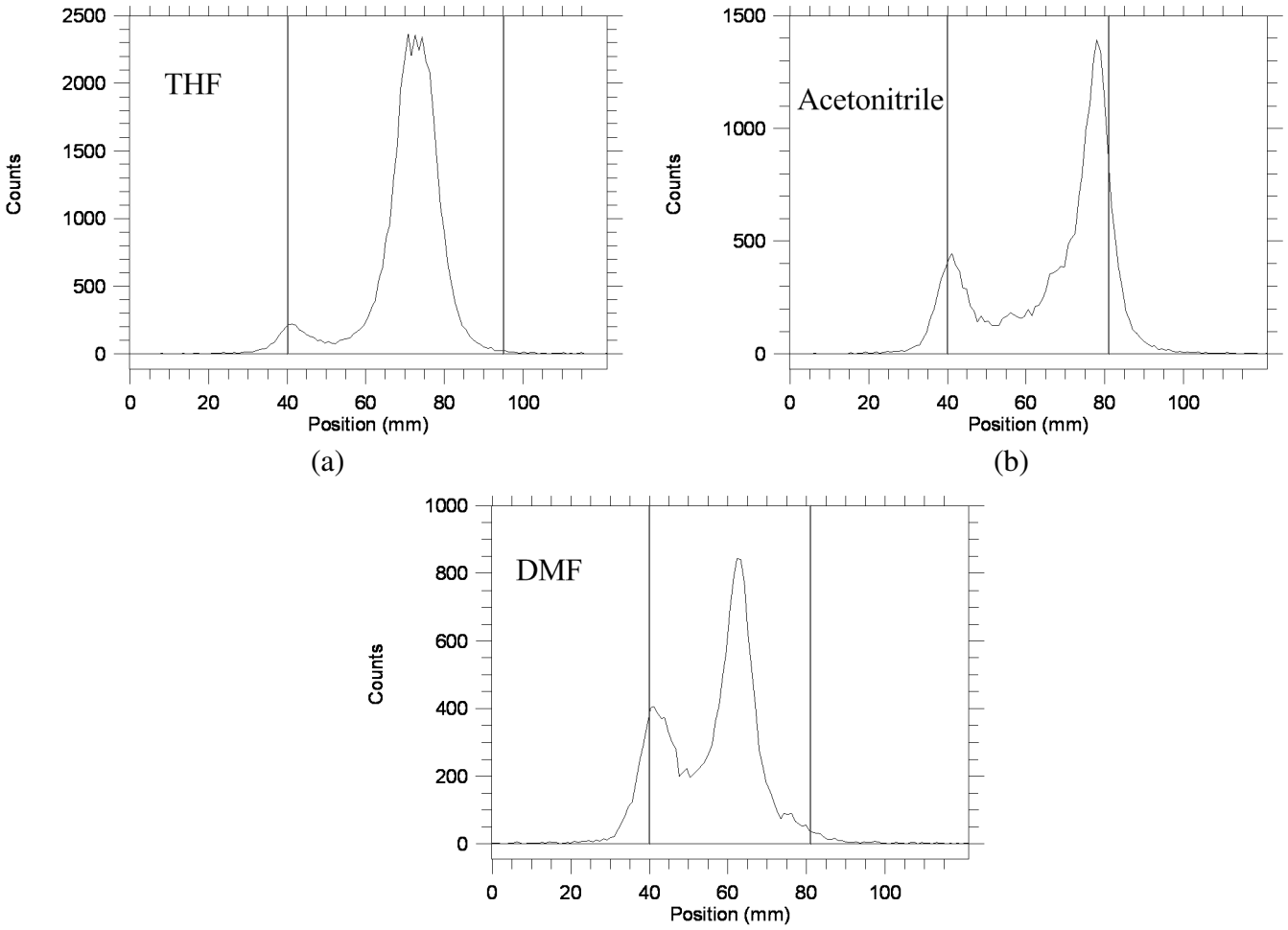


Figure S3. Radio-TLCs of control reactions using different solvents (a) THF (b) acetonitrile (c) DMF (Silica gel, 1:1 ethyl acetate/hexanes)

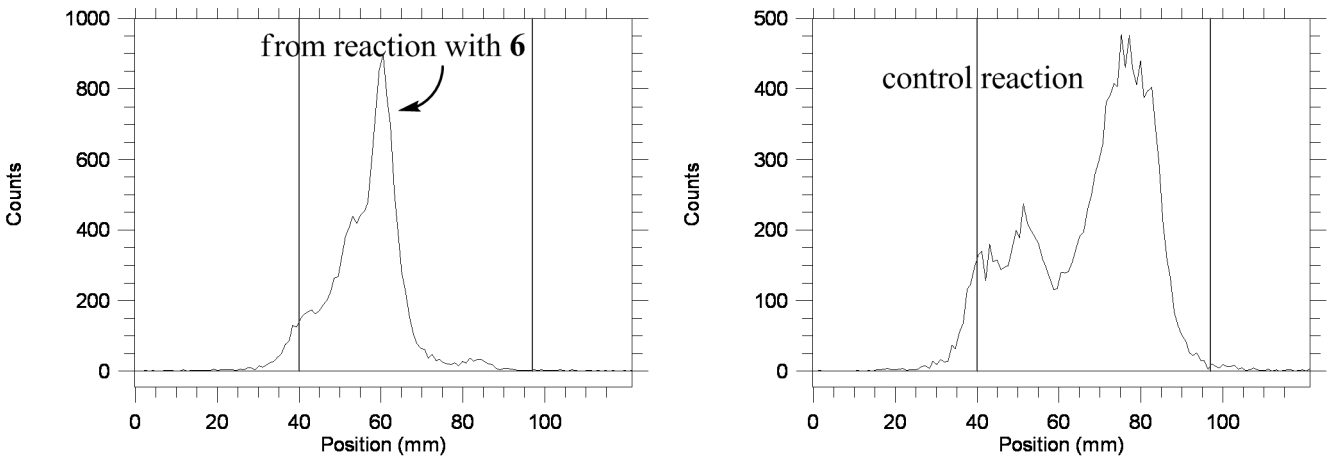
Reaction condition:

(a) ^{76}Br (dried, 20 μCi) in MeOH (10 μL), THF (200 μL), acetic acid (100 μL), PAA (1%) in MeOH (100 μL) (5 min);

(b) ^{76}Br (dried, 15 μCi) in MeOH (5 μL), MeCN (200 μL), acetic acid (50 μL), PAA (3%) in MeOH (100 μL) (10 min);

(c) ^{76}Br (dried, 15 μCi) in MeOH (5 μL), DMF (200 μL), acetic acid (50 μL), PAA (3%) in MeOH (100 μL) (10 min).

Note: A radioactive product was formed rapidly in the presence of THF, acetonitrile or DMF, respectively, in the above control reactions. These radioactive products were the same as those observed in the radiobromination of **4** or **5** when the above solvents were used.



(a) (b)

Figure S4. Radio-TLCs of radiobromination of **6** (a) and its control reaction (b) showing the formation of lipophilic byproducts (Silica gel, 1:12 ethyl acetate/hexanes)

Reaction condition:

(a) ^{76}Br in MeOH (10 µL), **6** (1.0 mg) in MeOH (100 µL), acetic acid (100 µL), PAA (1%) in acetic acid (100 µL);

(b) ^{76}Br in MeOH (10 µL), MeOH (100 µL), acetic acid (100 µL), PAA (1%) in acetic acid (100 µL).

Note: A major radioactive product (*panel a*) was observed in the reaction with tributyl precursor **6**; however, this product was more lipophilic than **6** according to the radio-TLC; this peak was not observed in the control reaction (*panel b*).

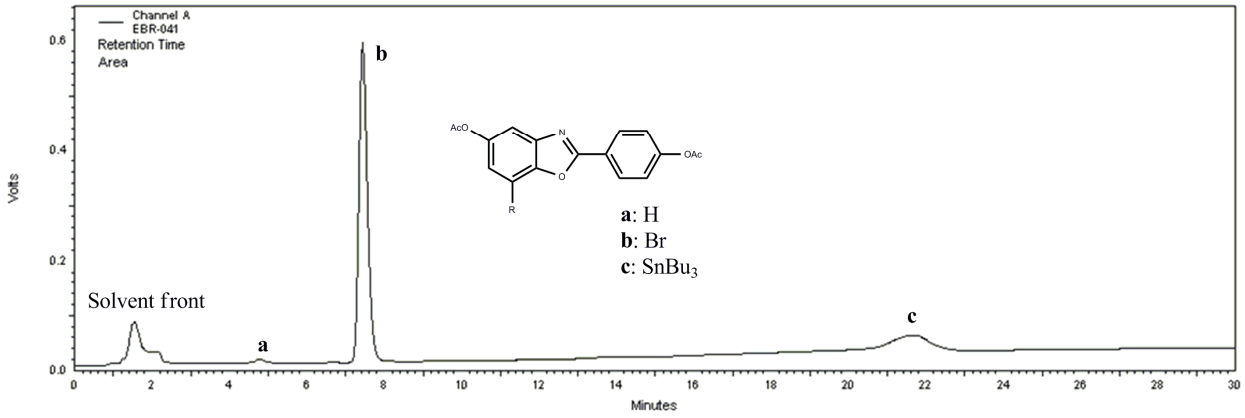


Figure S5. HPLC chromatograph of a non-radioactive synthesis of **2** from **4** using NH_4Br and PAA.

HPLC: Alltech Altima C18 250×4.6 mm 10µ, 285 nm, 2 mL/min; Gradient: Solvent A: Acetonitrile; Solvent B: ammonium formate buffer (0.1 M, pH = 4.5) A: 60%-90 % (0-20 min), 90% (20-30 min).

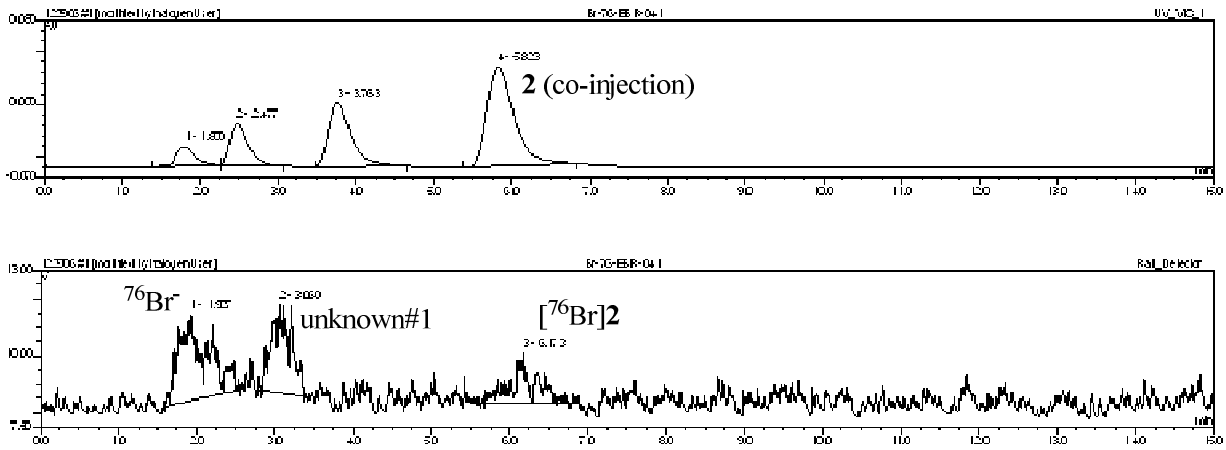


Figure S6. HPLC chromatographs of a reaction mixture from an attempted synthesis of [^{76}Br]**2** from **4**, showing [^{76}Br]Bromide, unknown #1, and [^{76}Br]**2** (co-injected with 2).

HPLC (Alltech Econosil, 250×4.6 mm, 10μ, 65% acetonitrile, 35% ammonium formate buffer (pH = 4.5), 2 mL/minun, 285 nm): [^{76}Br]bromide, t_R = 1.93 min, unknown #1, t_R = 3.06 min, [^{76}Br]**2**, t_R = 6.17 min, unknown #2 won't be eluted.