**Electronic supporting information (ESI)**

**General information**
GC analyses were carried out on a gas chromatograph (column, Rtx-200; 0.25 mm x 30 m) equipped with a mass selective detector operating at 70 eV (EI). GC/MS data were acquired on a GCMS-QP2020 NX (EI, 70 eV, carrier gas: He). Dry tetrahydrofuran and hexane were purchased from Kanto Chemical Co., Inc. or Fujifilm Wako Pure Chemicals and used without further purification. Stainless steel (SUS304) T-shaped micromixers with inner diameters of 250 μm were manufactured by Sanko Seiki Co., Inc. Stainless steel (SUS316) microtube reactors with inner diameter of 1000 μm purchased from GL Sciences were used unless otherwise stated. The micromixers and microtube reactors were connected with stainless steel fittings (GL Sciences, 1/16 OUW). The flow microreactor system was immersed in a cryogenic mixture bath with dry ice and acetone to control the temperature. Solutions were continuously introduced to the flow microreactor system using syringe pumps (Harvard PHD2000), equipped with gastight syringes purchased from SGE. All reactions were carried out under an atmosphere of argon. Lithium diisopropylamide (LDA) [1.09 M in hexane/THF] was purchased from Kanto Chemical Co., Inc. Exposure of diiodomethane to light should be minimized during all manipulations.

**General Procedure for lithiation of dihalomethane followed by the quench with methanol-$d_4$ using a flow microreactor system.**
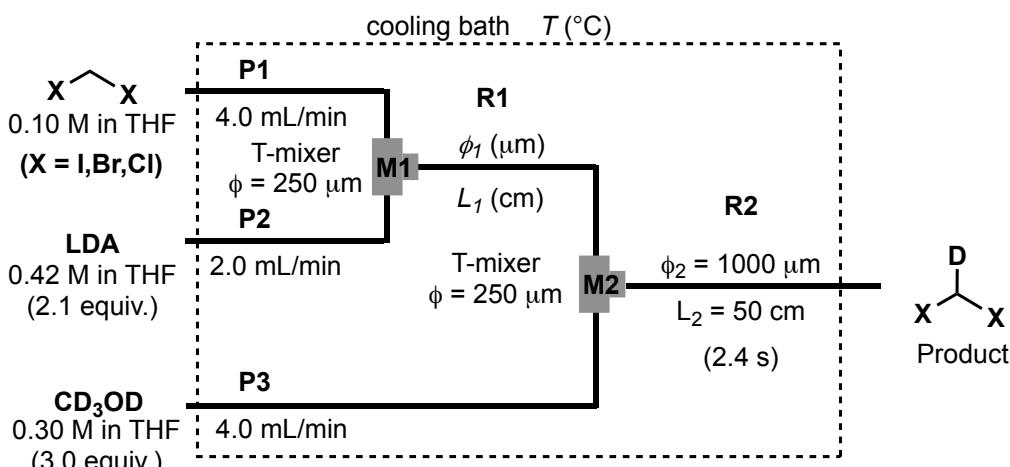


A flow microreactor system consisting of two T-shaped micromixers (**M1** and **M2**), two microtube reactors (**R1** and **R2**), and three tube precooling units (**P1**, **P2** and **P3** (inner diameter $\phi = 1000$ μm, length L = 100 cm)) was used. The flow microreactor system was dipped in a cooling bath (T °C). A solution of dihalomethane (diiodomethane (**1**), bromoiodomethane (**2**), chloroiodomethane (**3**), dibromomethane (**4**), bromochloromethane (**5**), dichloromethane (**6**)) (0.10 M in THF) (flow rate: 4.0 mL/min) and a solution of lithium diisopropylamide (LDA) (0.42 M in THF) (flow rate: 2.0 mL/min) were introduced to **M1** ($\phi = 250$ μm) by syringe pumps. The resulting solution was passed through **R1** and was mixed with a solution of methanol-$d_4$ (0.30 M in THF) (flow rate: 4.0 mL/min) in **M2** ($\phi = 250$ μm). The resulting solution was passed through **R2** ($\phi = 1000$ μm, L = 50 cm) ($t^{R2} = 2.4$ s)). After a steady state was reached, the outcoming solution was collected for 20 seconds in a vessel containing 4 mL of *sat. aq.* NH$_4$Cl. The yield of monodeuterated dihalomethane (**1-6-monoD**) was determined by GC/MS analysis using dodecane as an internal standard. The results obtained by changing the residence time and the temperature are summarized in Table S3.

**Yield and Deuteration estimation by GC/MS analysis**
Organic layer was analyzed by gas chromatography mass spectrometry. Recovery of diiodomethane (**5**), diiodomethane-$d_1$ (**6**), and diiodometahene-$d_2$ (**7**) were determined by GC analysis ($^tR$ 3.69 min) (initial oven temperature, 50 °C (5 min); temperature increase rate, 10 °C/min (15 min); final temperature, 200 °C) using an internal standard (dodecane). Ratio of **5**, **6**, and **7** were determined by GC/MS(EI) analysis considering isotopic distribution of mass peaks (for example, ratio of **6** was **6**/ (**5** + **6** + **7**)). Yield was calculated as follows: Yield = (recovery (%)) x (ratio of **Product** in **5**, **6**, and **7** (%)). The results are summarized in Table S1.

**Table S1.** Lithiation of dichloromethane (**1a**), dibromomethane (**1b**), diiodomethane (**1c**), chloroiodomethane (**1d**), and bromoiodomethane (**1e**) with LDA followed by trapping with methanol-$d_4$ using a flow microreactor system.

| Starting Material | Temperature [°C] | $L_1$ [cm] | $\phi_1$ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of **monoD** [%] | Yield of **monoD** [%] |
|---|---|---|---|---|---|---|---|
| **1a** | 0 | 3.5 | 1000 | 0.27 | 81 | 88 | 71 |
| | 0 | 12.5 | 1000 | 0.98 | 73 | 89 | 65 |
| | 0 | 50 | 1000 | 3.92 | 65 | 91 | 59 |
| | 0 | 100 | 1000 | 7.85 | 42 | 89 | 37 |
| | 0 | 200 | 1000 | 15.7 | 27 | 87 | 23 |
| | −20 | 3.5 | 500 | 0.069 | 99 | 46 | 46 |
| | −20 | 3.5 | 1000 | 0.27 | 99 | 86 | 85 |
| | −20 | 12.5 | 1000 | 0.98 | 99 | 88 | 87 |
| | −20 | 50 | 1000 | 3.92 | 99 | 88 | 87 |
| | −20 | 100 | 1000 | 7.85 | 99 | 87 | 86 |
| | −20 | 200 | 1000 | 15.7 | 87 | 85 | 74 |
| | −40 | 3.5 | 500 | 0.069 | 99 | 29 | 29 |
| | −40 | 3.5 | 1000 | 0.27 | 99 | 53 | 52 |
| | −40 | 12.5 | 1000 | 0.98 | 99 | 88 | 87 |
| | −40 | 50 | 1000 | 3.92 | 99 | 88 | 87 |
| | −40 | 100 | 1000 | 7.85 | 99 | 88 | 87 |
| | −40 | 200 | 1000 | 15.7 | 99 | 86 | 85 |
| | −60 | 3.5 | 500 | 0.069 | 99 | 24 | 24 |
| | −60 | 3.5 | 1000 | 0.27 | 99 | 36 | 36 |
| | −60 | 12.5 | 1000 | 0.98 | 99 | 60 | 59 |
| | −60 | 50 | 1000 | 3.92 | 99 | 83 | 82 |
| | −60 | 100 | 1000 | 7.85 | 99 | 84 | 83 |
| | −60 | 200 | 1000 | 15.7 | 99 | 85 | 84 |
| | −78 | 3.5 | 500 | 0.069 | 99 | 21 | 21 |
| | −78 | 3.5 | 1000 | 0.27 | 99 | 31 | 31 |
| | −78 | 12.5 | 1000 | 0.98 | 99 | 31 | 31 |
| | −78 | 50 | 1000 | 3.92 | 99 | 63 | 62 |
| | −78 | 100 | 1000 | 7.85 | 99 | 64 | 63 |
| | −78 | 200 | 1000 | 15.7 | 99 | 64 | 63 |

| Starting Material | Temperature [°C] | $L_1$ [cm] | $\phi_1$ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of **monoD** [%] | Yield of **monoD** [%] |
|---|---|---|---|---|---|---|---|
| **1b** | 0 | 3.5 | 1000 | 0.27 | 67 | 89 | 60 |
| | 0 | 12.5 | 1000 | 0.98 | 53 | 89 | 47 |
| | 0 | 50 | 1000 | 3.92 | 20 | 91 | 18 |
| | 0 | 100 | 1000 | 7.85 | 8 | 93 | 7 |
| | 0 | 200 | 1000 | 15.7 | 6 | 91 | 5 |
| | −20 | 3.5 | 500 | 0.069 | 99 | 84 | 83 |

| Starting Material | Temperature [°C] | $L_1$ [cm] | $\phi_1$ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of monoD [%] | Yield of monoD [%] |
|---|---|---|---|---|---|---|---|
| | −20 | 3.5 | 1000 | 0.27 | 99 | 87 | 86 |
| | −20 | 12.5 | 1000 | 0.98 | 99 | 89 | 88 |
| | −20 | 50 | 1000 | 3.92 | 75 | 89 | 67 |
| | −20 | 100 | 1000 | 7.85 | 60 | 91 | 55 |
| | −20 | 200 | 1000 | 15.7 | 47 | 90 | 42 |
| | −40 | 3.5 | 500 | 0.069 | 99 | 60 | 59 |
| | −40 | 3.5 | 1000 | 0.27 | 99 | 86 | 85 |
| | −40 | 12.5 | 1000 | 0.98 | 99 | 86 | 85 |
| | −40 | 50 | 1000 | 3.92 | 99 | 87 | 86 |
| | −40 | 100 | 1000 | 7.85 | 91 | 91 | 83 |
| | −40 | 200 | 1000 | 15.7 | 83 | 92 | 76 |
| | −60 | 3.5 | 500 | 0.069 | 99 | 48 | 48 |
| | −60 | 3.5 | 1000 | 0.27 | 99 | 64 | 63 |
| | −60 | 12.5 | 1000 | 0.98 | 99 | 70 | 69 |
| | −60 | 50 | 1000 | 3.92 | 99 | 76 | 75 |
| | −60 | 100 | 1000 | 7.85 | 98 | 89 | 87 |
| | −60 | 200 | 1000 | 15.7 | 92 | 89 | 82 |
| | −78 | 3.5 | 500 | 0.069 | 99 | 43 | 43 |
| | −78 | 3.5 | 1000 | 0.27 | 99 | 55 | 54 |
| | −78 | 12.5 | 1000 | 0.98 | 99 | 55 | 54 |
| | −78 | 50 | 1000 | 3.92 | 99 | 58 | 57 |
| | −78 | 100 | 1000 | 7.85 | 99 | 66 | 65 |
| | −78 | 200 | 1000 | 15.7 | 99 | 67 | 66 |

| Starting Material | Temperature [°C] | $L_1$ [cm] | $\phi_1$ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of monoD [%] | Yield of monoD [%] |
|---|---|---|---|---|---|---|---|
| **1c** | 0 | 3.5 | 500 | 0.069 | 66 | 93 | 61 |
| | 0 | 3.5 | 1000 | 0.27 | 64 | 94 | 60 |
| | 0 | 12.5 | 1000 | 0.98 | 18 | 96 | 17 |
| | 0 | 50 | 1000 | 3.92 | 3 | 53 | 2 |
| | 0 | 100 | 1000 | 7.85 | 3 | 30 | 1 |
| | 0 | 200 | 1000 | 15.7 | n.d. | n.d. | n.d. |
| | −20 | 3.5 | 500 | 0.069 | 99 | 85 | 84 |
| | −20 | 3.5 | 1000 | 0.27 | 86 | 92 | 79 |
| | −20 | 12.5 | 1000 | 0.98 | 71 | 94 | 67 |
| | −20 | 50 | 1000 | 3.92 | 29 | 95 | 28 |
| | −20 | 100 | 1000 | 7.85 | 12 | 94 | 11 |
| | −20 | 200 | 1000 | 15.7 | 6 | 77 | 5 |
| | −40 | 3.5 | 500 | 0.069 | 99 | 76 | 75 |
| | −40 | 3.5 | 1000 | 0.27 | 99 | 92 | 92 |
| | −40 | 12.5 | 1000 | 0.98 | 99 | 94 | 94 |
| | −40 | 50 | 1000 | 3.92 | 66 | 93 | 61 |

| Temperature [°C] | L₁ [cm] | φ₁ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of monoD [%] | Yield of monoD [%] |
|---|---|---|---|---|---|---|
| −40 | 100 | 1000 | 7.85 | 57 | 93 | 53 |
| −40 | 200 | 1000 | 15.7 | 31 | 93 | 29 |
| −60 | 3.5 | 500 | 0.069 | 99 | 40 | 40 |
| −60 | 3.5 | 1000 | 0.27 | 99 | 68 | 67 |
| −60 | 12.5 | 1000 | 0.98 | 99 | 78 | 77 |
| −60 | 50 | 1000 | 3.92 | 99 | 92 | 91 |
| −60 | 100 | 1000 | 7.85 | 93 | 93 | 86 |
| −60 | 200 | 1000 | 15.7 | 89 | 94 | 84 |
| −78 | 3.5 | 500 | 0.069 | 99 | 33 | 33 |
| −78 | 3.5 | 1000 | 0.27 | 99 | 44 | 44 |
| −78 | 12.5 | 1000 | 0.98 | 99 | 48 | 48 |
| −78 | 50 | 1000 | 3.92 | 99 | 79 | 78 |
| −78 | 100 | 1000 | 7.85 | 99 | 84 | 84 |
| −78 | 200 | 1000 | 15.7 | 99 | 91 | 90 |

| Starting Material | Temperature [°C] | L₁ [cm] | φ₁ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of monoD [%] | Yield of monoD [%] |
|---|---|---|---|---|---|---|---|
| **1d** | 0 | 3.5 | 1000 | 0.27 | 64 | 80 | 51 |
| | 0 | 12.5 | 1000 | 0.98 | 17 | 89 | 15 |
| | 0 | 50 | 1000 | 3.92 | 1 | 90 | 1 |
| | 0 | 100 | 1000 | 7.85 | n.d. | n.d. | n.d. |
| | 0 | 200 | 1000 | 15.7 | n.d. | n.d. | n.d. |
| | −20 | 3.5 | 500 | 0.069 | 91 | 79 | 72 |
| | −20 | 3.5 | 1000 | 0.27 | 93 | 88 | 82 |
| | −20 | 12.5 | 1000 | 0.98 | 96 | 91 | 87 |
| | −20 | 50 | 1000 | 3.92 | 48 | 89 | 43 |
| | −20 | 100 | 1000 | 7.85 | 26 | 90 | 23 |
| | −20 | 200 | 1000 | 15.7 | 14 | 91 | 13 |
| | −40 | 3.5 | 500 | 0.069 | 99 | 48 | 48 |
| | −40 | 3.5 | 1000 | 0.27 | 99 | 87 | 86 |
| | −40 | 12.5 | 1000 | 0.98 | 99 | 89 | 88 |
| | −40 | 50 | 1000 | 3.92 | 92 | 90 | 83 |
| | −40 | 100 | 1000 | 7.85 | 73 | 90 | 66 |
| | −40 | 200 | 1000 | 15.7 | 60 | 90 | 54 |
| | −60 | 3.5 | 500 | 0.069 | 99 | 31 | 31 |
| | −60 | 3.5 | 1000 | 0.27 | 99 | 47 | 47 |
| | −60 | 12.5 | 1000 | 0.98 | 99 | 59 | 58 |
| | −60 | 50 | 1000 | 3.92 | 99 | 85 | 84 |
| | −60 | 100 | 1000 | 7.85 | 99 | 89 | 88 |
| | −60 | 200 | 1000 | 15.7 | 99 | 89 | 88 |
| | −78 | 3.5 | 500 | 0.069 | 99 | 27 | 27 |
| | −78 | 3.5 | 1000 | 0.27 | 99 | 37 | 37 |
| | −78 | 12.5 | 1000 | 0.98 | 99 | 42 | 42 |
| | −78 | 50 | 1000 | 3.92 | 99 | 73 | 72 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | −78 | 100 | 1000 | 7.85 | 99 | 77 | 76 |
| | −78 | 200 | 1000 | 15.7 | 99 | 79 | 78 |

| Starting Material | Temperature [°C] | $L_1$ [cm] | $\phi_1$ [μm] | $t^{R1}$ [s] | Recovery [%] | Ratio of **monoD** [%] | Yield of **monoD** [%] |
|---|---|---|---|---|---|---|---|
| **1e** | 0 | 3.5 | 1000 | 0.27 | 68 | 90 | 61 |
| | 0 | 12.5 | 1000 | 0.98 | 40 | 91 | 36 |
| | 0 | 50 | 1000 | 3.92 | 8 | 93 | 7 |
| | 0 | 100 | 1000 | 7.85 | 1 | 77 | 1 |
| | 0 | 200 | 1000 | 15.7 | n.d. | n.d. | n.d. |
| | −20 | 3.5 | 500 | 0.069 | 99 | 88 | 87 |
| | −20 | 3.5 | 1000 | 0.27 | 93 | 89 | 83 |
| | −20 | 12.5 | 1000 | 0.98 | 81 | 90 | 73 |
| | −20 | 50 | 1000 | 3.92 | 49 | 90 | 44 |
| | −20 | 100 | 1000 | 7.85 | 29 | 91 | 26 |
| | −20 | 200 | 1000 | 15.7 | 7 | 92 | 6 |
| | −40 | 3.5 | 500 | 0.069 | 99 | 75 | 74 |
| | −40 | 3.5 | 1000 | 0.27 | 99 | 89 | 88 |
| | −40 | 12.5 | 1000 | 0.98 | 99 | 89 | 88 |
| | −40 | 50 | 1000 | 3.92 | 92 | 90 | 83 |
| | −40 | 100 | 1000 | 7.85 | 83 | 91 | 76 |
| | −40 | 200 | 1000 | 15.7 | 73 | 91 | 66 |
| | −60 | 3.5 | 500 | 0.069 | 99 | 40 | 40 |
| | −60 | 3.5 | 1000 | 0.27 | 99 | 70 | 69 |
| | −60 | 12.5 | 1000 | 0.98 | 99 | 85 | 84 |
| | −60 | 50 | 1000 | 3.92 | 99 | 88 | 87 |
| | −60 | 100 | 1000 | 7.85 | 99 | 90 | 89 |
| | −60 | 200 | 1000 | 15.7 | 99 | 90 | 89 |
| | −78 | 3.5 | 500 | 0.069 | 99 | 33 | 33 |
| | −78 | 3.5 | 1000 | 0.27 | 99 | 35 | 35 |
| | −78 | 12.5 | 1000 | 0.98 | 99 | 57 | 56 |
| | −78 | 50 | 1000 | 3.92 | 99 | 62 | 61 |
| | −78 | 100 | 1000 | 7.85 | 99 | 66 | 65 |
| | −78 | 200 | 1000 | 15.7 | 99 | 80 | 79 |

## Kinetic evaluation for decomposition rates of dihalomethyllithium intermediates

Kinetic rates are calculated from the plots based on Eq. S1 as depicted below.

$$\ln[\mathbf{7}]/[\mathbf{7}_{max}] = -k \cdot t^{R1} + C \quad \cdots \cdots (S1)$$

**2a** (LiCHCl$_2$)

0 °C — $y = -0.0741x - 0.3268$, $R^2 = 0.981$
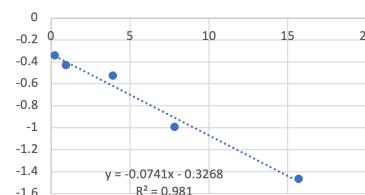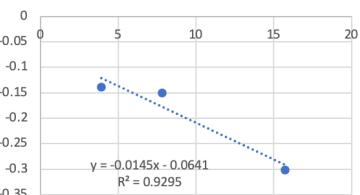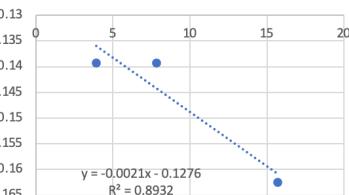
−20 °C — $y = -0.0145x - 0.0641$, $R^2 = 0.9295$

−40 °C — $y = -0.0021x - 0.1276$, $R^2 = 0.8932$

**2b** (LiCHBr$_2$)

0 °C — $y = -0.2838x - 0.4854$, $R^2 = 0.9936$

−20 °C — $y = -0.0674x - 0.0885$, $R^2 = 0.9702$

−40 °C — $y = -0.0106x - 0.1068$, $R^2 = 0.9975$

**2c** (LiCHI$_2$)

0 °C — $y = -1.5008x - 0.2659$, $R^2 = 0.9604$

−20 °C — $y = -0.2913x - 0.127$, $R^2 = 0.9983$

−40 °C — $y = -0.0809x - 0.0531$, $R^2 = 0.871$

**2d** (LiCHClI)

0 °C — $y = -1.0286x - 0.6159$, $R^2 = 0.9844$

−20 °C — $y = -0.1918x - 0.0017$, $R^2 = 0.9867$

−40 °C — $y = -0.0426x - 0.0661$, $R^2 = 0.9588$

**2e** (LiCHBrI)

0 °C — $y = -0.6003x - 0.3632$, $R^2 = 0.9992$

−20 °C — $y = -0.1494x - 0.1921$, $R^2 = 0.9951$

−40 °C — $y = -0.0214x - 0.1052$, $R^2 = 0.9988$
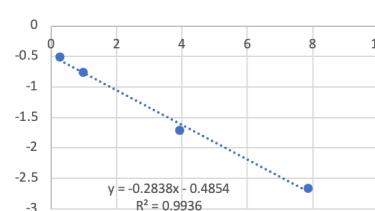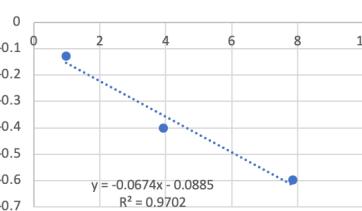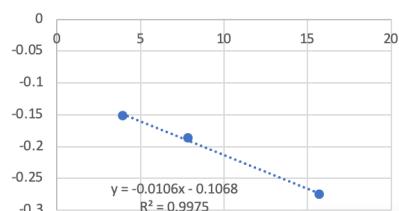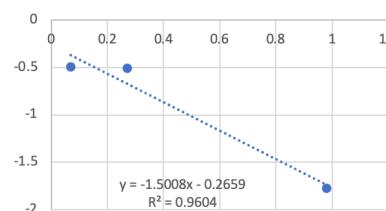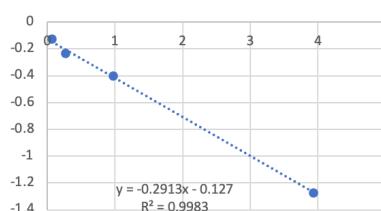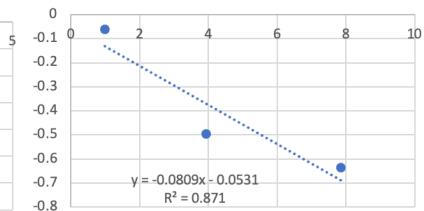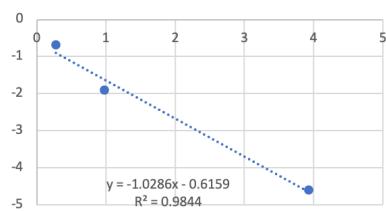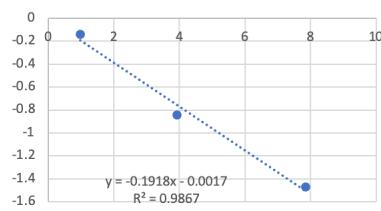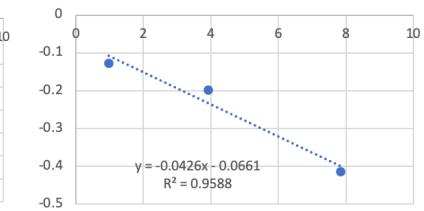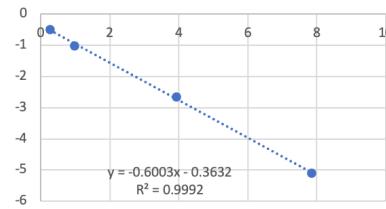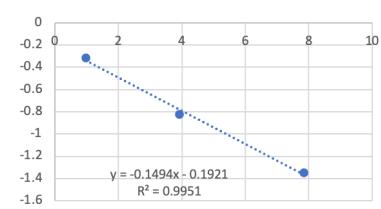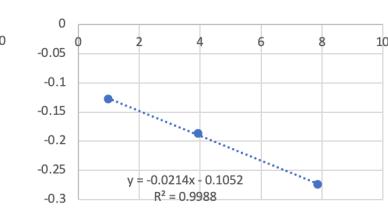
**Fig. S1** Kinetic plots corresponding to the decomposition of dihalomethyllithium species. [**7**] = (concentration of **7a-e**), [**7**$_{max}$] = (theoretical maximum concentration of **7a-e**) ~ [**1**$_0$] = (initial concentration of **1a-e**). All plots for **7a-e** at 0, −20, −40 °C are drawn in the figures above. Vertical axis: ln[**7**]/[**7**$_{max}$], horizontal axis: residence time $t^{R1}$ (s)

## Theoretical calculations

Geometries for all compounds have been optimized by the MP2/6-31+G(d) level of theory. Accurate bond energies have been obtained by the CCSD(T)[1] single-point energy calculations with aug-cc-pVDZ[2] and aug-cc-pVDZ-PP[3] basis sets for the normal and iodine atom respectively. All calculations have been carried out with Gaussian16[4] program. The calculated dissociation energies of dihalomethyllithium ($\Delta E_0$) are listed with total energy and zero-point energy (ZPE) for each molecule/radical in Table S4.

**Table S2.** Calculated energies

|  | total energy [a.u.] | ZPE [a.u.] | $\Delta E_0$ [kcal/mol] |
|---|---|---|---|
| LiCHI-I | −635.71057 | 0.01608 | 58.6 |
| LiCHI | −340.83023 | 0.01306 | |
| I | −294.78387 | 0.00000 | |
| LiCHBr-Br | −5191.16297 | 0.01659 | 65.8 |
| LiCHBr | −2618.55023 | 0.01296 | |
| Br | −2572.50419 | 0.00000 | |
| LiCHCl-Cl | −965.40465 | 0.01768 | 72.6 |
| LiCHCl | −505.67064 | 0.01326 | |
| Cl | −459.61390 | 0.00000 | |
| LiCHBr-I | −2913.46550 | 0.01644 | 80.3 |
| LiCHBr | −2618.55023 | 0.01296 | |
| I | −294.78387 | 0.00000 | |
| LiCHCl-I | −800.57547 | 0.01717 | 73.5 |
| LiCHCl | −505.67064 | 0.01326 | |
| I | −294.78387 | 0.00000 | |

## References

1.  J. A. Pople, M. Head-Gordon, K. Raghavachari, *J. Chem. Phys.* 1987, **87**, 5968.
2.  T. H. Dunning, *J. Chem. Phys.* 1989, **90**, 1007.
3.  K. A. Peterson, D. Figgen, M. Dolg, H. Stoll, *J. Chem. Phys.* 2007, **126**, 124101.
4.  M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.