

# Selective, Scalable Synthesis of C<sub>60</sub>-Fullerene/Indene Monoadducts Using a Microwave Flow Applicator

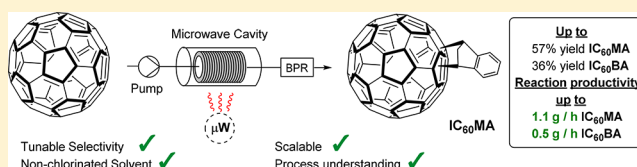
Joshua P. Barham,<sup>\*,†,‡,§</sup> Satoko Tanaka,<sup>†</sup> Emiko Koyama,<sup>†</sup> Noriyuki Ohneda,<sup>‡</sup> Tadashi Okamoto,<sup>‡</sup> Hiromichi Odajima,<sup>‡</sup> Jun-ichi Sugiyama,<sup>†</sup> and Yasuo Norikane<sup>\*,†</sup>

<sup>†</sup>National Institute of Advanced Industrial Science and Technology, Tsukuba Central 5, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8568, Japan

<sup>‡</sup>SAIDA FDS, INC., 143-10 Isshiki, Yaizu, Shizuoka 425-0054, Japan

## Supporting Information

**ABSTRACT:** The synergy of continuous processing and microwave heating technologies has unlocked scalable (g/h), safe and efficient reaction conditions for synthesis of fullerene/indene-based organic photovoltaic acceptor materials in a nonchlorinated solvent with levels of productivity unparalleled by previous syntheses. The microwave flow reactor sustains high temperature while employing short residence times, reaction conditions which uniquely allow the selective synthesis of fullerene/indene monoadducts. Design of experiments analysis revealed residence time as the most crucial factor for conversion and selectivity control.



## INTRODUCTION

Polymer solar cells (PSCs) use a blend film of polymer electron donor and C<sub>60</sub>-fullerene derivative electron acceptor, sandwiched between an anode (typically indium titanium oxide) and a low work function metal cathode (for example, aluminum).<sup>1,2</sup> Poly(3-hexylthiophene) (P3HT) and phenyl-C<sub>61</sub>-butyric acid methyl ester (PCBM) are widely used PSC donor and acceptor materials, respectively. In 2010, indene-C<sub>60</sub> monoadduct (IC<sub>60</sub>MA) and indene-C<sub>60</sub> bisadduct (IC<sub>60</sub>BA) were identified as superior to PCBM as PSC components, due to their higher LUMO energy levels, resulting in higher open-cell voltages (V<sub>oc</sub>).<sup>3,4</sup> A key factor behind the success of IC<sub>60</sub>MA and IC<sub>60</sub>BA has been their enhanced solubility;<sup>4</sup> this increases miscibility with polymer donors<sup>5</sup> and PSC formulation via solution processing is advantageous.<sup>6</sup> In addition to PSCs, IC<sub>60</sub>MA was recently employed in perovskite solar cells.<sup>7</sup> The widespread application of IC<sub>60</sub>MA and IC<sub>60</sub>BA has been limited by the following:

- (1) Their cumbersome synthesis: an electronically mismatched Diels–Alder reaction between C<sub>60</sub> and indene, which requires elevated temperatures, polychlorinated aromatic solvents and extended reaction times.
- (2) The herculean purification required to separate IC<sub>60</sub>MA, IC<sub>60</sub>BA and unreacted C<sub>60</sub> due to the poor solubility of C<sub>60</sub> in most organic solvents.<sup>8</sup>

Reactions are normally conducted in batch mode using sealed vessels and thermal heating<sup>3,9,10</sup> or using microwave (MW) heating;<sup>11</sup> such methods possess limited scalability (up to 0.04 g/h;<sup>3</sup> Table 1 entry 2). Furthermore, although high-boiling polychlorinated aromatic solvents (1,2-dichlorobenzene (1,2-DCB) and 1,2,4-trichlorobenzene (1,2,4-TCB)) are typically employed due to the increased solubility of C<sub>60</sub>, they are

persistent environmental pollutants<sup>12,13</sup> and are cost-ineffective on a large scale. Continuous processing (CP) is globally recognized as a promising technology that is now established in multiple chemical industries: functional materials,<sup>14,15</sup> pharmaceuticals,<sup>16–18</sup> petrochemical and fine/commodity chemicals.<sup>19</sup> CP has clear benefits over traditional batch processing in terms of cost, safety, synthetic maneuverability, process robustness, reproducibility and scalability. CP has been used to produce a PCBM derivative on a microchip<sup>20</sup> and Wong, Jones and co-workers recently reported elegant CP methods for synthesis of fullerene derivatives, including conditions delivering up to 0.07 g/h of IC<sub>60</sub>BA (Table 1 entry 6).<sup>21</sup>

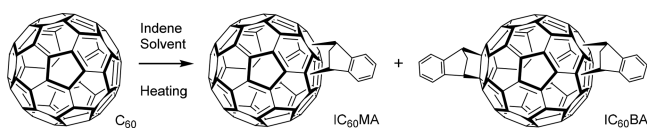
The benefits of CP for the scale-up of C<sub>60</sub>-fullerene acceptor material synthesis (and benefits of MW for accelerating the synthesis in batch) have been summarized in a recent review.<sup>22</sup> Herein, we report a scalable, safe and efficient continuous process for fullerene conjugation in a nonchlorinated solvent, using a commercially available MW flow reactor system (Figure 1),<sup>23a,b</sup> where conditions can be tuned to selectively deliver up to 1.1 g/h of IC<sub>60</sub>MA or 0.5 g/h of IC<sub>60</sub>BA.

## RESULTS AND DISCUSSION

The commercial MW flow reactor system in question is similar to that previously disclosed,<sup>23a</sup> with some modifications (see Supporting Information for full details). First, toluene was investigated as a nonhalogenated aromatic solvent. At 190 °C, the flowing reaction mixture had changed color from purple to dark brown and a 57% yield of IC<sub>60</sub>MA was observed (Table 2 entry 1). Increasing the temperature while holding other conditions constant resulted in a loss of mass balance,

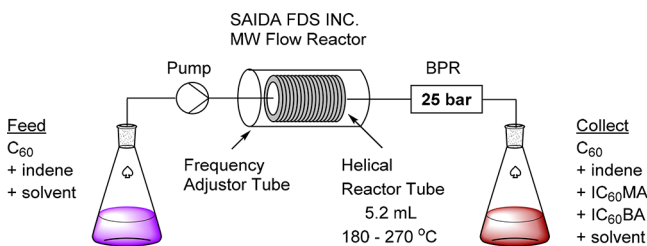
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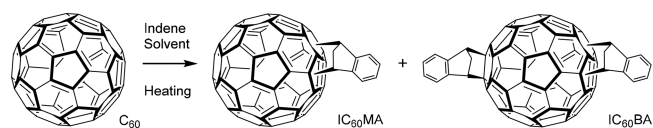
**Table 1. Previous C<sub>60</sub>/Indene Conjugation Reports Versus This Work<sup>a</sup>**

entry <sup>b</sup>	method, heating	solvent	temp (°C)	yield (%)		IC <sub>x</sub> A <sup>c</sup> (g/h)
				IC <sub>60</sub> MA	IC <sub>60</sub> BA	
1 <sup>8</sup>	B(720), <sup>d</sup> T <sup>e</sup>	DCB	180	35	ND	ND <sup>f</sup>
2 <sup>3</sup>	B(720), T	TCB	220	25	34	0.04 <sup>g</sup>
3 <sup>3</sup>	B(720), T	DCB	180	ND	26	0.04 <sup>h</sup>
4 <sup>11</sup>	B(5), MW <sup>i</sup>	DCB	180	49	29	0.03 <sup>h</sup>
5 <sup>11</sup>	B(5), MW	DCB	180	35	62	0.04 <sup>g</sup>
6 <sup>21</sup>	F(0.1), <sup>j</sup> T	DCB	200	ND	54	0.07 <sup>h</sup>
7 <sup>k,l</sup>	F(1), MW	<i>o</i> -xyl	190	52	24	0.13 <sup>g</sup>
8 <sup>k,m</sup>	F(5), MW	<i>o</i> -xyl	190	57	17	0.74 <sup>g</sup>
9 <sup>k,n</sup>	F(5), MW	<i>o</i> -xyl	270	40	32	0.47 <sup>h</sup>
10 <sup>k,o</sup>	F(12), MW	<i>o</i> -xyl	270	40	7	1.07 <sup>g</sup>

<sup>a</sup>*o*-xyl, *o*-xylene. ND, not determined. <sup>b</sup>See references. <sup>c</sup>IC<sub>60</sub>MA or IC<sub>60</sub>BA productivity (g/h). Batch productivities are calculated from isolated yield and total reaction time. Flow productivities are calculated from HPLC yield and flow rate. <sup>d</sup>B, batch; reaction time (min) is shown in parentheses. <sup>e</sup>T, thermal heating. <sup>f</sup>Scale of operation unspecified. <sup>g</sup>Refers to IC<sub>60</sub>MA. <sup>h</sup>Refers to IC<sub>60</sub>BA. <sup>i</sup>MW, microwave heating. <sup>j</sup>F, flow; flow rate (mL/min) is shown in parentheses. <sup>k</sup>This work. <sup>l</sup>Conditions A, Table 2 entry 5. <sup>m</sup>Conditions B, Table 3 entry 7. <sup>n</sup>Conditions C, Table 3 entry 8. <sup>o</sup>Conditions D, Table 5 entry 4.

**Figure 1.** Reactor configuration for the CP synthesis of C<sub>60</sub>/indene adducts using a MW applicator.

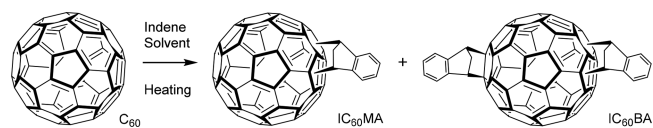
presumably via decomposition (Table 2 entries 2 and 3). Although the solubility of C<sub>60</sub> in PhMe is 4.0 mM at 25 °C,<sup>8</sup> C<sub>60</sub> exhibits counterintuitive behavior whereby its solubility decreases with increasing temperature in certain solvents.<sup>24a-c</sup> Operating at 0.7 mM C<sub>60</sub> resulted in precipitation (Table 2 entry 4); thus, 0.5 mM was identified as the maximum operating C<sub>60</sub> concentration in PhMe, producing 0.01 g/h under these conditions. Gratifyingly, by employing *o*-xylene the maximum operating C<sub>60</sub> concentration could be increased to 5.4 mM, yet with similar conversion and IC<sub>60</sub>MA yield (Table 2 entry 5). A commercially available mixture “xylenes” (min 80% cGC assay of *o*-, *m*-, *p*-xylenes) as solvent gave precipitation under the same conditions (Table 2 entry 7), highlighting the importance of ortho-substitution in enhancing C<sub>60</sub> solubility (reported C<sub>60</sub> solubility is 7.0 mM in xylenes at 25 °C).<sup>8,25</sup> Use of *o*-DCB, as commonly employed in previous syntheses, gave a similar result to *o*-xylene under the same conditions. However, operating at 25.0 mM C<sub>60</sub> in *o*-DCB gave precipitation (reported C<sub>60</sub> solubility is 38.0 mM in *o*-DCB at 25 °C).<sup>8</sup> Results indicate that *o*-DCB can be substituted by *o*-xylene without compromising yield or productivity.<sup>26</sup> Due to the ~10× higher C<sub>60</sub> concentration accessible in *o*-xylene than in

**Table 2. IC<sub>60</sub>MA, IC<sub>60</sub>BA and Recovered C<sub>60</sub> Yields (%) Varying [C<sub>60</sub>] and Solvent<sup>a</sup>**

entry	[C <sub>60</sub> ] (mM)	solvent	temp <sup>b</sup> (°C)	yield <sup>c</sup> (%)		
				C <sub>60</sub>	IC <sub>60</sub> MA	IC <sub>60</sub> BA
1	0.5	PhMe	190	14	57	19
2	0.5	PhMe	200	13	52	16
3	0.5	PhMe	220	1	8	5
4 <sup>d</sup>	0.7	PhMe	180			
5 <sup>e</sup>	5.4	<i>o</i> -xyl	190	21	52 [53] <sup>f</sup>	24
6	5.4	<i>o</i> -xyl	200	25	50	18
7	5.4	xylenes	175			
8	5.4	<i>o</i> -DCB	190	19	49	17
9	5.4	<i>o</i> -DCB	190			

<sup>a</sup>DCB, 1,2-dichlorobenzene. *o*-xyl, *o*-xylene. All reactions used 0.4 M indene and a 0.9 mL/min flow rate, with a 5.8 min residence time (*R*<sub>T</sub>). <sup>b</sup>Reaction temperature measured at the reactor tube exit upon reaching steady state. <sup>c</sup>Yield determined by HPLC; see Supporting Information for details. <sup>d</sup>Reactor blocked at the temperature specified due to a black precipitate. <sup>e</sup>Average of two replicates. These conditions were identified as Conditions A. <sup>f</sup>Yield in parentheses determined by <sup>1</sup>H NMR spectroscopic analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene (10 mol %) as an internal standard.

PhMe, IC<sub>60</sub>MA productivity (0.13 g/h) was ~10× higher than that in PhMe (0.01 g/h). Next, the effects of indene concentration and residence time were investigated. Doubling indene concentration increased C<sub>60</sub> conversion (Table 3 entry 1 vs Table 2 entry 6), while halving indene concentration led to unstable flow rates and loss of mass balance (Table 3 entry 2 vs Table 2 entry 6), possibly due to precipitation of C<sub>60</sub>. Decreasing residence time from *R*<sub>T</sub> = 5.8 min to *R*<sub>T</sub> = 2.2

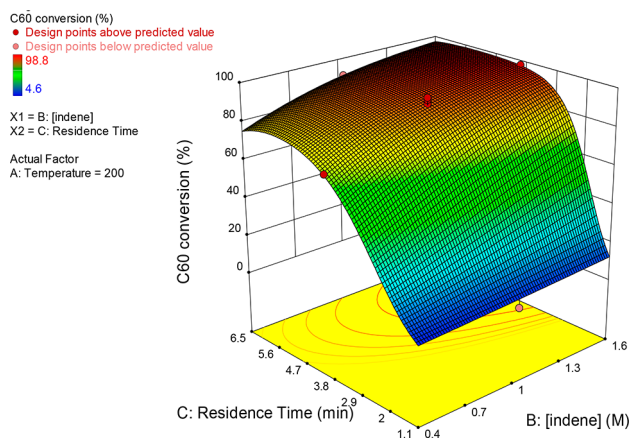
**Table 3. IC<sub>60</sub>MA, IC<sub>60</sub>BA and Recovered C<sub>60</sub> Yields (%) Varying Flow Rate and [Indene]<sup>a</sup>**

entry	[indene] (M)	<i>R</i> <sub>T</sub> (min)	temp <sup>b</sup> (°C)	yield <sup>c</sup> (%)		
				C <sub>60</sub>	IC <sub>60</sub> MA	IC <sub>60</sub> BA
1	0.8	5.8	200	11	48	36
2 <sup>d</sup>	0.2	5.8	200	23	14	3
3	0.4	2.2	200	62	18	1
4 <sup>e</sup>	0.8	2.2	200	29	58	18
5 <sup>e</sup>	0.8	2.2	220	38	54	12
6 <sup>e</sup>	0.8	1.1	220	92	10	0
7 <sup>f</sup>	0.8	1.1	270	25	57	17
8 <sup>g</sup>	1.6	1.1	270	6	40	32

<sup>a</sup>*R*<sub>T</sub>, residence time. All reactions used 5.4 mM C<sub>60</sub> and *o*-xylene as solvent. <sup>b</sup>Reaction temperature measured at the reactor tube exit upon reaching steady state. <sup>c</sup>Yield determined by HPLC; see Supporting Information for details. <sup>d</sup>Reactor exhibited unstable flow rates, suggesting precipitation. <sup>e</sup>Here, mass balances exceed 100% but are within ±5%, thus deemed acceptably within error of the HPLC quantification method. <sup>f</sup>Identified as Conditions B. <sup>g</sup>Identified as Conditions C.

min drastically decreased  $C_{60}$  conversion (Table 3 entry 3 vs Table 2 entry 6). At 2.4 mL/min, doubling indene concentration restored  $C_{60}$  conversion (Table 3 entry 4). However, at 4.8 mL/min ( $R_T = 1.1$  min), the reaction was almost completely shut down (Table 3 entry 5 vs entry 6).

Increasing temperature to 270 °C restored  $C_{60}$  conversion and higher indene concentration could be employed to promote conversion of  $IC_{60}MA$  to  $IC_{60}BA$  (Table 3 entries 7 and 8, Conditions B and C). Using this low residence time of 1.1 min, productivity of  $IC_{60}MA$  reached 0.74 g/h (Table 1 entry 8, Conditions B) and that of  $IC_{60}BA$  reached 0.47 g/h (Table 1 entry 9, Conditions C). This productivity of  $IC_{60}BA$  is >5× higher than that achieved by a thermal flow system previously reported<sup>21</sup> and is to our knowledge the highest ever reported. Table 3 clearly identifies temperature, indene concentration and  $R_T$  as key factors in the conversion of  $C_{60}$  to  $IC_{60}MA/IC_{60}BA$ . To optimize the reaction further, it was deemed important to compare the relative importance of such factors and to identify any possible multifactor interactions. Therefore, we turned to design of experiment (DoE) techniques.<sup>27</sup> In the first instance, a two-level full factorial analysis identified that residence time ( $R_T$ ) exerted the most influence on  $C_{60}$  conversion. Across the design space studied, temperature and indene concentration were less important factors and multifactor interactions were generally insignificant. See Supporting Information for the full analysis and graphs. The two-level full factorial DoE analysis sufficed to compare factors but could not be used for prediction due to its inability to model data curvature. Therefore, the two-level full factorial model was augmented with additional experiments to construct a face-centered central composite model,<sup>28</sup> which allowed accurate predictions to be made within the design space (Figure 2). Two predictions were made based on the model and validated by experiment (see Table 4).



**Figure 2.** Response surface plot for  $C_{60}$  conversion (%) at 200 °C as a function of residence time (min) and [indene] (M).

The influence of residence time can be clearly seen from the response surface and it is much greater than the influence of indene concentration and temperature. Strong correlations were observed between  $C_{60}$  conversion and (i)  $IC_{60}BA$  yield and (ii)  $ICMA/IC_{60}BA$  ratio. In conjunction with the face-centered central composite model (Figure 2), this allows prediction of  $IC_{60}BA$  yield and  $ICMA/IC_{60}BA$  ratio from a given set of reaction conditions (see Supporting Information for full details and graphs). Notably, it was in these DoE studies that one of the

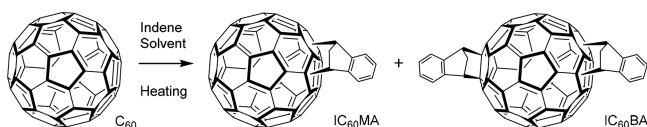
**Table 4.**  $C_{60}$  Conversion (%) Predicted from Response Surface Versus Experimental Result<sup>a</sup>

entry	$R_T$ (min)	temp <sup>b</sup> (°C)	conv (%)		yield <sup>c</sup> (%)	
			$C_{60}$	$IC_{60}MA$	$IC_{60}MA$	$IC_{60}BA$
1 <sup>c</sup>	3.1	210	86	47	25	
2 <sup>d</sup>	3.1	210	92	52	33	
3 <sup>c</sup>	2.5	200	64	52	9	
4 <sup>d</sup>	2.5	200	66	50	9	

<sup>a</sup> $R_T$ , residence time. Conv, conversion. All reactions used 5.4 mM  $C_{60}$ , 1.6 M indene and *o*-xylene as solvent. <sup>b</sup>Reaction temperature measured at the reactor tube exit upon reaching steady state. <sup>c</sup>Predicted result using face-centered central composite model for  $C_{60}$  conversion.  $IC_{60}MA$  and  $IC_{60}BA$  yields were predicted using the predicted  $C_{60}$  conversion and reading off calibration curves; see Supporting Information for details. <sup>d</sup>Experimental result, conversion and yields determined by HPLC; see Supporting Information for details.

facets of MW heating (rapid heating and cooling)<sup>23a</sup> was realized. Upon changing reaction conditions, a new stable temperature was achieved within ~5 min on average. This accelerated data acquisition toward reaction optimization demonstrates a key advantage of the MW flow system.

Longer residence times were desirable for  $C_{60}$  conversion, yet could not be achieved without decreasing the flow rate (compromising productivity) within the boundaries of the reactor equipment used herein. A decision was made to identify the maximum productivity achievable in the current system by using high temperature (up to 270 °C) and high indene concentration (up to 1.6 M) to counterbalance the impact of high flow rate (low  $R_T$ ). However, at flow rates greater than 6.0 mL/min, it was not possible to reach 270 °C by operating the 250 W MW source at full power. Therefore, a custom 1 000 W MW source was employed. This 1 000 W MW reactor, which gave comparable results to the 250 W MW flow reactor setup under the same conditions (Table 5 entry 1 vs entry 2), successfully achieved 270 °C at up to 11.6 mL/min flow rate ( $R_T = 0.4$  min).<sup>29</sup> Albeit at the sacrifice of  $C_{60}$  conversion and  $IC_{60}MA$  yield,  $IC_{60}MA$  productivity reached 1.12 g/h (Table 5 entry 5). Conditions D were employed for 1.2 h, affording 1.1 g of  $IC_{60}MA$  (35%) after isolation (Table 5 entry 4). This productivity of  $IC_{60}MA$  is ~30× higher than that reported by Li and co-workers<sup>3</sup> and is to our knowledge the highest ever reported. Furthermore,  $IC_{60}MA$  selectivity observed in this study is higher than ever reported before (up to 6:1  $IC_{60}MA/IC_{60}BA$ , Table 5 entry 4).<sup>30</sup> This monoadduct selectivity enhancement is likely due to the shorter residence times employed herein, which allows less time for the reaction of  $IC_{60}MA$  with a second molecule of indene.<sup>31–33</sup> While we successfully isolated 1.11 g of  $IC_{60}MA$  by standard silica chromatography, purification of fullerene derivatives is still a key issue in the field, which generally requires multiple attempts and can be time- and solvent-intensive. Overall, our study tackles productivity at the reaction step, an equally key issue especially given recent interest in mixed fullerene acceptor blends,<sup>10</sup> for which the reaction step is the bottleneck. Under Conditions A,  $IC_{70}MA$  and novel compound  $IC_{60}MA$ -chloro were successfully synthesized in 38% and 53% yields,

Table 5. Establishing Maximum IC<sub>60</sub>MA Productivity<sup>a</sup>

entry	$R_T$ (min)	temp <sup>b</sup> (°C)	yield <sup>c</sup> (%)			IC <sub>60</sub> MA <sup>d</sup> (g/h)
			C <sub>60</sub>	IC <sub>60</sub> MA	IC <sub>60</sub> BA	
1 <sup>e</sup>	0.9	260	10	46	23	0.74
2 <sup>f</sup>	0.9	260	26	46	11	0.69
3	0.9	270	20	47	15	0.72
4 <sup>g,h</sup>	0.5	270	36	40 [35]	7	1.07
5	0.4	270	40	36	5	1.12

<sup>a</sup> $R_T$ , residence time. All reactions used 5.4 mM C<sub>60</sub>, 1.6 M indene and *o*-xylene as solvent. <sup>b</sup>Reaction temperature measured at the reactor tube exit upon reaching steady state. <sup>c</sup>Yield determined by HPLC; see Supporting Information for details. <sup>d</sup>Flow productivities are calculated from HPLC yield and flow rate (see Supporting Information). <sup>e</sup>Using the 250 W MW flow reactor setup, operating at full power. <sup>f</sup>Using the 1 000 W MW flow reactor setup, controlling power as necessary to maintain desired temperature. <sup>g</sup>Identified as Conditions D. <sup>h</sup>Isolated yield in parentheses; 1.11 g of IC<sub>60</sub>MA was isolated on gram-scale after employing Conditions D for 1.2 h.

respectively, confirming the robustness of the CP reaction conditions (Figure 3). The productivity of IC<sub>70</sub>MA under Conditions A was 0.11 g/h (in comparison, 0.07 g/h IC<sub>70</sub>BA was achieved in *o*-DCM in the previously reported thermal flow system).<sup>21</sup>

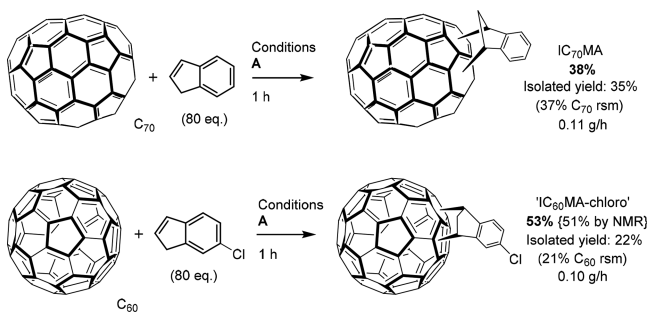


Figure 3. CP synthesis of IC<sub>70</sub>MA and IC<sub>60</sub>MA-chloro. Yields determined by HPLC; see Supporting Information for details.

In conclusion, we report a scalable, safe and efficient continuous synthesis of photovoltaic cell components IC<sub>60</sub>MA and IC<sub>60</sub>BA using a nonchlorinated solvent by means of a commercially available MW flow reactor system. The ability to rapidly change reaction temperature by MW heating accelerated data acquisition for reaction optimization. DoE analysis revealed residence time as the most crucial factor influencing C<sub>60</sub> conversion and a face-centered central composite design model was constructed and successfully used for result prediction. A characteristic benefit to the MW flow reactor is its ability to employ short residence times while sustaining high temperature, translating to synthesis of IC<sub>60</sub>MA in higher selectivity (up to 6:1) and productivity (1.1 g/h) than ever before, although it could be tuned to also deliver high productivities of IC<sub>60</sub>BA (0.5 g/h). By using *o*-xylene as a substitute solvent for chlorinated aromatics, we demonstrated an improvement in the “greenness” of fullerene/indene adduct synthesis.<sup>34</sup> The robustness of our system was demonstrated via

the synthesis of IC<sub>60</sub>MA on gram-scale and the synthesis of IC<sub>70</sub>MA and IC<sub>60</sub>MA-chloro, which are currently under testing in solar cell device applications. Future efforts will investigate different reactor designs,<sup>35</sup> particularly with longer reaction tube volumes that will allow longer residence times ( $R_T$ ) without compromising flow rate.

## EXPERIMENTAL SECTION

**General Experimental.** Unless specified otherwise, batch reactions were carried out under an inert (N<sub>2</sub>) atmosphere. Cryogenic conditions (−78 °C) were achieved using dry ice/acetone baths. Temperatures of 0 °C were obtained by means of an ice bath. Room temperature (rt) indicates temperatures in the range of 20–25 °C. HPLC analyses were performed using a modular JASCO HPLC system comprising a JASCO PU-2089 Plus quaternary gradient pump and a JASCO MD-2015 Plus multiwavelength UV detector. The analytical column (TSKgel CN-80Ts column, 5 μM, 4.6 mm × 250 mm), housed within a JASCO CO-4060 air blow thermostat maintained at 40 °C, was eluted with a mobile phase consisting of 1% CHCl<sub>3</sub>/hexane at a flow rate of 1.0 mL/min, with UV monitoring at 300 nm. Data were acquired using JASCO ChromNAV software. For purposes of thin-layer chromatography (TLC), silica gel 60N aluminum plates were used, with UV light (λ = 254 and 365 nm) used for visualization. Purification was achieved by column chromatography, using silica gel 60N with a particle size of 100–210 μm. In some cases, purification was achieved by preparative gel permeation chromatography (GPC), using a LC908-C60 instrument fitted with a combination of JAIGEL 1H-40 and JAIGEL 2H-40 columns, using CHCl<sub>3</sub> as eluent (flow rate = 4.7 mL/min) and following with a UV detector (λ = 254 nm). Removal of solvents (in vacuo) was achieved using rotary evaporators. For NMR spectroscopy, chloroform-d (D 99.8% + 0.05% v/v TMS) was used. All NMR data were collected using a Bruker Avance 400 instrument using 400 and 101 MHz and for <sup>1</sup>H and <sup>13</sup>C NMR, respectively. Fourier transformations of the data were carried out using Topspin. Peak picking, integration and multiplicity were obtained using NMR software by Hiroshi Nakamura (Emeritus Professor, University of Hokkaido). Reference values for residual solvents were taken as δ = 7.27 (CDCl<sub>3</sub>) and 2.60 ppm (toluene-*d*<sub>6</sub>) for <sup>1</sup>H NMR; δ = 77.00 ppm (CDCl<sub>3</sub>) for <sup>13</sup>C NMR. Multiplicities for coupled signals were denoted as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, apt. = apparent, dd = double doublet, etc. Coupling constants (*J*) are given in Hz and are uncorrected. Where appropriate, COSY, DEPT, HSQC, and HMBC experiments were carried out to aid assignment. Infrared spectra were recorded on a PerkinElmer Spectrum 2000 FTIR either as a thin film cast on a KBr disc or as a pressed KBr disc (for fullerene-containing molecules). UV–visible absorption measurements were performed using a PerkinElmer Lambda 700 UV/vis/NIR spectrophotometer. All samples were prepared at 1.0 × 10<sup>−5</sup> M. Matrix-assisted laser desorption/ionization time-of-flight mass (MALDI-TOF-MS) spectrometry was performed on a Bruker Daltonics autoflex III spectrometer with 9,10-diphenylanthracene as the matrix and using PhMe for dissolution (1,8,9-trihydroxyanthracene was used as the matrix for IC<sub>60</sub>MA-chloro). For IC<sub>60</sub>MA-chloro, high-resolution MALDI-TOF-MS was recorded using a JMS-S3000 MALDI spiral TOF-MS. 2-[(2*E*)-3-(4-*tert*-Butylphenyl)-2-methyl-2-prop-2-enylidene]malononitrile (DCTB) was used for the matrix. For 6-chloro-1*H*-indene, high-resolution mass spectral (HRMS) analyses were carried out on a JEOL MStation JMS 700 V (resolution (*m*/Δ*m*) = 3000). All solvents and reagents were purchased and used as supplied or purified using standard techniques.<sup>36</sup> Analytical standards of C<sub>60</sub>, IC<sub>60</sub>BA and IC<sub>60</sub>MA were purchased.

**General Procedure for C<sub>60</sub>/Fullerene Microwave Flow Reaction.** Continuous flow experiments were conducted using a commercially available microwave flow reactor; see Supporting Information for details. Prior to conducting any reaction, the flow rate was set and the actual flow rate was measured using solvent only to ensure consistency. All residence times ( $R_T$ ) quoted are calculated from the actual measured flow rate, not the set flow rate. The

adjustable back pressure regulator (BPR) was set to ensure pressures between 2.0 and 3.0 MPa. Because of the reactor's operational thresholds, reactions were never allowed to exceed 3.0 MPa and reactor exit temperature (as measured by the thermocouple) was never allowed to exceed 300 °C. A PTFE frequency adjustor tube (o.d. = 26.0 mm, i.d. = 22.0 mm, length = 200.0 mm) enclosed the helical reactor tube and the size of the MW cavity was adjusted such as to bring the MW absorption frequency within 2.4–2.5 GHz, with the peak maxima lying between 2.44 and 2.46 GHz, as measured by a radiofrequency analyzer device. C<sub>60</sub> fullerene (or C<sub>70</sub>), indene (or other indene derivative) and *o*-xylene (or other solvent) were mixed in the specified amounts to prepare a C<sub>60</sub> fullerene solution of known concentration. The resultant mixture was sonicated until clear from particles (~2 h), vacuum-filtered using filter paper (no visual precipitate or agglomerates were observed in the filter paper), covered in foil and passed through the microwave flow reactor at the specified flow rate, heating to the specified temperature (by selecting an appropriate MW power, predetermined by heating tests processing *o*-xylene only at various flow rates and MW power settings). This temperature was that measured by a temperature probe at the reactor tube exit. Once stable temperature had been reached, the reaction mixture was discarded to waste until >1 residence time had passed. The actual flow rate was measured again upon reaching stable temperature. For HPLC yields, an aliquot of reaction mixture of known volume and concentration was collected. The aliquot was diluted with *o*-xylene to prepare a 1 mM solution. By comparison with authentic standards (1 mM in *o*-xylene), HPLC was used to determine the yields of C<sub>60</sub>, IC<sub>60</sub>MA and IC<sub>60</sub>BA (see Supporting Information). For NMR yields, an aliquot of reaction mixture of known volume and concentration was collected and concentrated to dryness in vacuo and 1,3,5-trimethoxybenzene (10 mol %, based on the theoretical mol of C<sub>60</sub> fullerene present calculated from the initial C<sub>60</sub> concentration) was added. The sample was dissolved in toluene-*d*<sub>8</sub> and the yield was determined by <sup>1</sup>H NMR (see Supporting Information). For isolations, a known volume of reaction mixture was collected at stable temperature (the flow rate quoted for the reaction was determined by the total volume collected over the time period of collection, so it is an average flow rate), concentrated to dryness in vacuo and purified by column chromatography (a gradient of CHCl<sub>3</sub>/hexane, as specified) to afford the products.

**Indene-C<sub>60</sub> Monoadduct.** According to the general procedure, to C<sub>60</sub> fullerene (3.92 g, 5.44 mmol) was added indene (186.0 mL, 1.60 mol, 294 equiv) and *o*-xylene (814.0 mL) to prepare a 5.4 mM solution in C<sub>60</sub>. The resultant mixture was sonicated until clear (~2 h), filtered, covered in foil and passed through the microwave flow reactor at 9.9 mL/min heating to 270 °C (260–300 W). Once stable temperature had been reached, 10 mL of reaction mixture was discarded to waste (>1 residence time) and then a 10 mL aliquot of reaction mixture was collected. A further 0.2 mL of reaction mixture was collected and diluted with 0.8 mL of *o*-xylene to prepare a 1 mM solution. By comparison with authentic IC<sub>60</sub>MA (1 mM in *o*-xylene), HPLC revealed a 40% yield of IC<sub>60</sub>MA. The 10 mL aliquot was concentrated to dryness in vacuo. Purification by column chromatography (a gradient of CHCl<sub>3</sub>/hexane 20:1 to 5:1) gave IC<sub>60</sub>MA as a dark brown solid (14.7 mg, 17.6 μmol, 35% based on the theoretical max 54.0 μmol collected); IR ν<sub>max</sub> (KBr pellet) 2959–2848, 1559, 1541, 1459, 1425, 1262, 1232, 1213 cm<sup>-1</sup> (authentic standard C<sub>69</sub>H<sub>8</sub> ν<sub>max</sub> (KBr pellet) 1559, 1541, 1460, 1426, 1262, 1232, 1215 cm<sup>-1</sup>); UV–vis (CHCl<sub>3</sub>): λ<sub>max</sub> = 319, 329, 432 nm (authentic standard C<sub>69</sub>H<sub>8</sub> λ<sub>max</sub> = 310, 329, 432 nm); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.65 (2H, dd, *J* = 5.3, 3.1 Hz, CH), 7.45 (2H, dd, *J* = 5.4, 3.1 Hz, CH), 4.96 (2H, t, *J* = 1.6 Hz, CH), 3.86 (1H, dt, *J* = 10.0 Hz, 1.5 Hz, CH<sub>2</sub>), 2.94 (1H, dt, *J* = 10.1 Hz, 1.7 Hz, CH<sub>2</sub>); <sup>13</sup>C NMR (the remaining peaks of the C<sub>60</sub> unit could not be observed) (101 MHz, CDCl<sub>3</sub>) δ 156.4, 155.1, 147.2, 146.3, 146.2, 3 × 146.1, 146.0, 145.8, 2 × 145.4, 145.2, 145.0, 144.6, 144.4, 143.1, 142.8, 142.7, 142.5, 142.3, 142.2, 142.1, 142.0, 2 × 141.8, 140.1, 139.7, 137.6, 137.4, 127.4, 124.0, 75.6, 58.1, 46.1; MS–MALDI *m/z* calculated for C<sub>69</sub>H<sub>8</sub>, 836.06; found, 836.25 (authentic standard C<sub>69</sub>H<sub>8</sub>, found, 836.29). Purity was confirmed by HPLC

(>95% IC<sub>60</sub>MA). Data are consistent with literature<sup>37</sup> and the authentic IC<sub>60</sub>MA standard.

**Indene-C<sub>60</sub> Monoadduct Gram-Scale Synthesis.** According to the general procedure, to C<sub>60</sub> fullerene (3.776 g, 5.24 mmol) was added indene (179.0 mL, 1.54 mol, 294 equiv) and *o*-xylene (783.0 mL) to prepare a 5.4 mM solution in C<sub>60</sub>. The resultant mixture was sonicated until clear (~2 h), filtered, covered in foil and passed through the microwave flow reactor at 9.9 mL/min heating to 270 °C (295–315 W). Once stable temperature had been reached, 10 mL of reaction mixture was discarded to waste (>1 residence time). A further 0.2 mL of reaction mixture was collected and diluted with 0.8 mL *o*-xylene to prepare a 1 mM solution. By comparison with authentic IC<sub>60</sub>MA (1 mM in *o*-xylene), HPLC revealed a 41% yield of IC<sub>60</sub>MA. Then, a 753 mL aliquot of reaction mixture was collected at stable temperature. After collection, HPLC revealed a 45% yield of IC<sub>60</sub>MA. The 753 mL aliquot was concentrated to dryness in vacuo. Purification by column chromatography (a gradient of CHCl<sub>3</sub>/hexane 20:1 to 5:1) gave IC<sub>60</sub>MA as a dark brown solid; 1.11 g, 33% (based on the theoretical max 4.07 mmol collected). Characterization data matched that above and purity was confirmed by HPLC (>95% IC<sub>60</sub>MA).

**Indene-C<sub>70</sub> Monoadduct.** According to the general procedure, to C<sub>70</sub> fullerene (500.0 mg, 0.59 mmol) was added indene (5.5 mL, 47.2 mmol, 80 equiv) and *o*-xylene (103.5 mL) to prepare a 5.4 mM solution in C<sub>70</sub>. The resultant mixture was sonicated until clear (~2 h), filtered, covered in foil and passed through the microwave flow reactor at 0.9 mL/min heating to 190 °C (130 W). Once stable temperature had been reached, 10 mL of reaction mixture was discarded to waste (>1 residence time) and then the reaction mixture was collected for 1 h (54.0 mL aliquot, overall flow rate 0.9 mL/min). A further 0.2 mL of reaction mixture was collected and diluted with 0.8 mL of *o*-xylene to prepare a 1 mM solution. By comparison with authentic IC<sub>70</sub>MA (1 mM in *o*-xylene), HPLC revealed a 38% yield of IC<sub>70</sub>MA. The 54.0 mL aliquot was concentrated to dryness in vacuo. Purification by column chromatography (a gradient of CHCl<sub>3</sub>/hexane 20:1 to 5:1) gave IC<sub>70</sub>MA as a black solid (96.3 mg, 100.7 μmol, 35% based on the theoretical max 291.6 μmol collected); IR ν<sub>max</sub> (KBr pellet) 2963–2849, 1559, 1541, 1457, 1419, 1326, 1263, 1232, 1212 cm<sup>-1</sup>; UV–vis (CHCl<sub>3</sub>): λ<sub>max</sub> = 330, 399, 460 nm; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.73–7.02 (4H, m, CH), 4.77–2.09 (4H, m, CH, CH<sub>2</sub>); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 159.0, 151.4–125.9 (multiple peaks indicating C<sub>70</sub> unit), 124.9, 124.5, 124.0, 123.9, 123.7, 119.8, 68.6, 66.7, 58.1, 55.4, 46.1, 44.4, 39.0, 37.6, 32.5, 31.7; MS–MALDI *m/z* calculated for C<sub>79</sub>H<sub>8</sub>, 956.06; found, 956.26. The potential for different IC<sub>70</sub>MA isomers to form under different conditions led to discrepancies with the literature NMR data.<sup>38</sup> For compounds where regioisomers occur, complex NMR data and discrepancies between literature are commonly reported in the literature.<sup>38,39</sup> Purity was confirmed by HPLC (>95% IC<sub>70</sub>MA, <5% C<sub>70</sub> by quantification by comparison with an authentic C<sub>70</sub> standard at same concentration) and identity was confirmed by MALDI-MS.

**6-Chloro-1*H*-indene.** Reduction of 5-chloro-1-indanone was conducted according to a literature procedure.<sup>40</sup> A reaction flask was charged with 5-chloro-1-indanone (13.5 g, 81.0 mmol) and a 1:1 mixture of 1,2-dichloroethane/methanol (320 mL). NaBH<sub>4</sub> (6.1 g, 161.4 mmol, 2.0 equiv) was added to the stirred mixture and the resulting clear, colorless solution was allowed to stir open to air for 30 min while evolution of gas ceased. The reaction mixture was washed into a separatory funnel with CHCl<sub>3</sub> (300 mL) and water (300 mL). The layers were separated and the aqueous layer was extracted with further CHCl<sub>3</sub> (2 × 300 mL). The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated in vacuo to yield 5-chloro-2,3-dihydro-1*H*-inden-1-ol as a pale-yellow oil (14.3 g), observed as a single compound by <sup>1</sup>H NMR. This crude product was carried through to the next step. Elimination to afford 6-chloro-1*H*-indene was conducted according to a literature procedure.<sup>40</sup> Crude 5-chloro-2,3-dihydro-1*H*-inden-1-ol was dissolved in PhMe (450 mL) and *p*-TsOH monohydrate (446 mg, 2.3 mmol, 3 mol %) was added. The reaction was heated at reflux for 2.5 h with azeotropic removal of H<sub>2</sub>O (Dean–Stark conditions). After cooling to rt, the mixture was neutralized with saturated aqueous NaHCO<sub>3</sub> (100 mL) and washed into a separatory

funnel with EtOAc (200 mL). The layers were separated and the aqueous layer was extracted with further EtOAc (3 × 200 mL). The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated in vacuo to yield a pale-brown oil (12.8 g), which was purified by column chromatography (hexane) to afford 6-chloro-1*H*-indene as a colorless oil (10.0 g, 82%); IR  $\nu_{\max}$  (neat) 3129–2764 (C–H), 1606 (Ar), 1583 (Ar), 1547 (Ar), 1457, 1416, 1389, 1357, 1327, 1288, 1270, 1225, 1204 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.45 (1H, br. s, CH), 7.31 (1H, d, *J* = 7.9 Hz, CH), 7.27–7.24 (1H, m, CH), 6.86–6.84 (1H, m, CH), 6.58–6.56 (1H, m, CH), 3.40 (2H, s, CH<sub>2</sub>); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  145.4 (C), 143.3 (C), 134.6 (CH), 131.4 (CH), 130.6 (C), 126.4 (CH), 124.4 (CH), 121.6 (CH), 39.0 (CH<sub>2</sub>); HRMS *m/z* calculated for C<sub>9</sub>H<sub>7</sub>Cl ([M]<sup>+</sup>), 150.0236; found, 150.0237. <sup>1</sup>H and <sup>13</sup>C NMR data are consistent with the literature.<sup>41</sup>

**5-Chloro-indene-C<sub>60</sub> Monoadduct.** According to the general procedure, to C<sub>60</sub> fullerene (705 mg, 0.98 mmol) was added 6-chloro-1*H*-indene (10.8 g, ~9.9 mL, 0.072 mol, 73 equiv) and *o*-xylene (170.1 mL) to prepare a 5.4 mM solution in C<sub>60</sub>. The resultant mixture was sonicated until clear (~2 h), filtered, covered in foil and passed through the microwave flow reactor at 0.9 mL/min heating to 190 °C (130 W). Once stable temperature had been reached, 10 mL of reaction mixture was discarded to waste (>1 residence time) and then the reaction mixture was collected for 1 h (38.5 mL aliquot, overall flow rate 0.6 mL/min). A further 0.2 mL of reaction mixture was collected and diluted with 0.8 mL of *o*-xylene to prepare a 1 mM solution. By comparison with pure 5-chloro-indene-C<sub>60</sub> monoadduct (IC<sub>60</sub>MA-chloro) obtained following purification (1 mM in *o*-xylene), HPLC revealed a 53% yield of IC<sub>60</sub>MA-chloro. The 38.5 mL aliquot was concentrated to dryness in vacuo. A further 2.5 mL of reaction mixture was collected and concentrated to dryness before adding 1,3,5-trimethoxybenzene (2.3 mg, 10 mol %). <sup>1</sup>H NMR revealed a 51% yield of IC<sub>60</sub>MA-chloro. Purification by column chromatography (a gradient of CHCl<sub>3</sub>/hexane 20:1 to 5:1) gave IC<sub>60</sub>MA-chloro as a dark-brown solid (39.5 mg, 45.3  $\mu$ mol, 22% based on the theoretical max 209.4  $\mu$ mol collected); IR  $\nu_{\max}$  (KBr pellet) 2967–2850, 1718, 1600, 1578, 1559, 1541, 1463, 1427, 1386, 1322, 1279, 1260, 1213 cm<sup>-1</sup>; UV–vis (CHCl<sub>3</sub>):  $\lambda_{\max}$  = 319, 329, 432 nm; <sup>1</sup>H NMR (400 MHz, tol-*d*<sub>8</sub>\*)  $\delta$  7.46–7.12 (3H, m, CH), 7.15 (1H, d, *J* = 8.6 Hz, CH), 6.91 (1H, d, *J* = 8.6 Hz, CH), 6.47–6.41 (1H, m, CH), 4.58–4.01 (1H, m, CH) 3.83–2.97 (2H, m, CH), 2.85–2.81 (1H, m, CH<sub>2</sub>), 2.78–2.70 (1H, m, CH<sub>2</sub>), 2.32–2.25 (1H, m, CH<sub>2</sub>), 1.90–1.97 (1H, m, CH<sub>2</sub>); <sup>13</sup>C NMR (the remaining peaks of the C<sub>60</sub> unit could not be observed) (101 MHz, tol-*d*<sub>8</sub>\*)  $\delta$  153.2, 147.0, 146.4, 145.2, 144.8, 138.8, 138.7, 138.3, 138.2, 134.0, 131.5, 130.3, 129.5, 128.2, 128.1, 128.0, 127.9, 126.8, 126.7, 125.7, 125.5, 125.4, 122.3, 47.9, 39.6, 39.1, 35.0, 32.7, 31.4; MS (HR-MALDI-TOF MS): *m/z* calculated for C<sub>69</sub>H<sub>7</sub>Cl<sup>+</sup>, 870.0231; found, 870.0235. Isotope pattern matched that simulated (see Supporting Information). Purity was confirmed by HPLC and identity was confirmed by MALDI-MS. Note: NMR data in CDCl<sub>3</sub> could not be obtained due to insufficient solubility; therefore, NMR spectra were obtained in toluene-*d*<sub>8</sub>.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b03209.

MW flow reactor details, HPLC methods, DoE studies, MW versus thermal heating flow reaction results, HPLC elugrams, NMR spectra and MS-MALDI spectra of fullerene derivatives (PDF)

## ■ AUTHOR INFORMATION

### Corresponding Authors

\*E-mail: j.barham@saidagroup.jp.

\*E-mail: y-norikane@aist.gov.jp.

## ORCID

Joshua P. Barham: 0000-0003-1675-9399

## Notes

The authors declare no competing financial interest.

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(24) The dependence of C<sub>60</sub> solubility on temperature has been the subject of numerous studies. For selected papers, see: (a) Korobov, M. V.; Mirakyan, A. L.; Avramenko, N. V.; Olofsson, G.; Smith, A. L.; Ruoff, R. S. *J. Phys. Chem. B* **1999**, *103*, 1339–1346. (b) Kulkarni, P. P.; Jafvert, C. T. *Environ. Sci. Technol.* **2008**, *42*, 845–851. (c) Kolker, A. M.; Kozlov, A. V. *Russ. J. Phys. Chem. A* **2012**, *86*, 715–719.

(25) The remarkably enhanced ability of *ortho*-substitution in di- or trisubstituted aromatic solvents on their C<sub>60</sub> solubility has been reported previously, see ref 24c and Scrivens, W. A.; Tour, J. M. *J. Chem. Soc., Chem. Commun.* **1993**, *0*, 1207–1209.

(26) An insightful reviewer suggested trifluorotoluene as a candidate alternative solvent that benefits from a lower boiling point than *o*-xylene and has shown favorable properties over toluene for MW reactions. For examples, see: (a) Smith, J. A.; Jones, R. K.; Booker, G. W.; Pyke, S. M. *J. Org. Chem.* **2008**, *73*, 8880–8892. (b) Veiga, A. X.; Arenz, S.; Erdélyi, M. *Synthesis* **2013**, *45*, 777–784.

(27) Weissman, S. A.; Anderson, N. G. *Org. Process Res. Dev.* **2015**, *19*, 1605–1633.

(28) For an example application of the face-centred central composite model in reaction optimization, see: Sanderson, J. N.; Dominey, A. P.; Percy, J. M. *Adv. Synth. Catal.* **2017**, *359*, 1007–1017.

(29) At elevated reaction temperatures, thermal expansion of reactor material and reaction mixture has been reported as having a significant effect on residence time, see: Martin, R. E.; Morawitz, F.; Kuratli, C.; Alker, A. M.; Alanine, A. I. *Eur. J. Org. Chem.* **2012**, *2012*, 47–52. Because of the SAIDA FDS, Inc., MW flow reactor design, such effects were negligible in the study herein. See [Supporting Information](#) for further details and discussion.

(30) Performance of fullerene/indene bisadducts as solar cell components exhibits variability due to the number of geometrical and regioisomers involved, which in turn varies depending on reaction conditions and purification method, see: Zhang, B.; Subbiah, J.; Jones, D. J.; Wong, W. W. H. *Beilstein J. Org. Chem.* **2016**, *12*, 903–911. Fullerene/indene monoadducts do not suffer such variability; thus, selective synthetic methods for their synthesis are desirable.

(31) Here, selectivity is described for reactions that had >60% C<sub>60</sub> conversion and gave rise to IC<sub>60</sub>MA in useful (≥40%) yield.

(32) IC<sub>60</sub>TA (triadduct) and equivalent analogues were not detected by HPLC or MS-MALDI of the reaction mixture.

(33) The selectivity enhancement for IC<sub>60</sub>MA herein is due to *short residence time* and is not a consequence of a “microwave effect”. A microwave effect was ruled out by (i) permittivity measurements, (ii) investigations using pulsed MW and (iii) comparison of a MW heating and thermal heating flow reaction; see [Supporting Information](#).

(34) There could be potential to operate the reaction in indene as solvent (neat). Solubility of C<sub>60</sub> in indene was measured at 6.7 mM (vs 7.0 mM in xylenes reported in ref 25) at 25 °C. However, DoE studies showed that increasing indene concentration from 0.4 to 1.6 M gave only a limited benefit. Use of indene as solvent was considered less cost-effective (especially for custom indene derivatives), less practical (due to indene’s high boiling point) and less general than *o*-xylene as solvent and was not attempted herein.

(35) Helical tube reactors exhibit many benefits over straight tube reactors, which were not investigated herein. The shape of the helical

tube reactor lends itself to secondary flows. Such behavior increases radical mixing and inhibits turbulence relative to a straight reactor, see: (a) Wang, H.; Mustaffar, A.; Phan, A. N.; Zivkovic, V.; Reay, D.; Law, R.; Boodhoo, K. *Chem. Eng. Process.* **2017**, *118*, 78–107. (b) Hüttl, T. J.; Friedrich, R. J. *Int. J. Heat Fluid Flow* **2000**, *21*, 345–353. In addition, because helical tube reactors accommodate larger volumes than straight tube reactors in the same sized MW cavity, productivity would be compromised by decreasing flow rate to achieve similar residence times to the helical tube reactor. Moreover, the combination of smaller reactor volume and low permittivity of aromatic hydrocarbon solvents gives rise to poorer absorption (thus, greater reflection) of MW power inside the cavity, which is undesirable from a safety and device longevity perspective. For a discussion of helical vs straight tubes in continuous flow microwave-heated chemistry, see ref 23a.

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