JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Article
pubs.acs.org/JACS

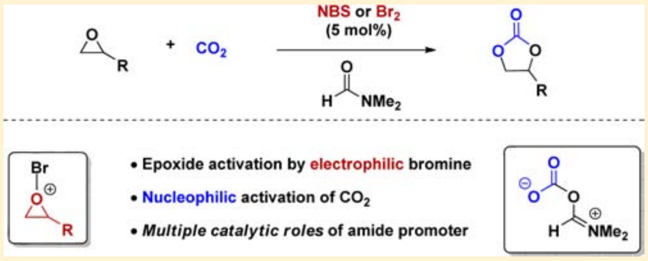
Bromine-Catalyzed Conversion of CO_2 and Epoxides to Cyclic Carbonates under Continuous Flow Conditions

Jennifer A. Kozak,[†,§] Jie Wu,[†,§] Xiao Su,[‡] Fritz Simeon,[‡] T. Alan Hatton,*[,‡] and Timothy F. Jamison*[,†]

[†]Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139 United States
[‡]Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States

Supporting Information

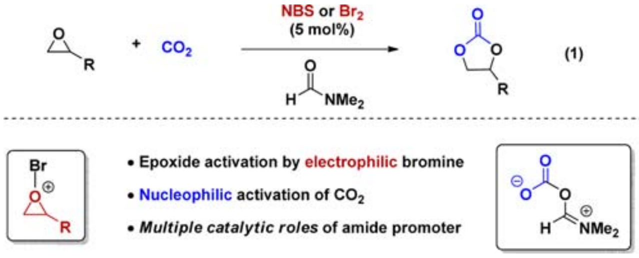
ABSTRACT: A continuous method for the formation of cyclic carbonates from epoxides and carbon dioxide (CO_2) is described. The catalysts used are inexpensive and effective in converting the reagents to the products in a residence time (t_R) of 30 min. The cyclic carbonate products are obtained in good to excellent yield (51−92%). On the basis of a series of kinetics experiments, we propose a reaction mechanism involving epoxide activation by electrophilic bromine and CO_2 activation by an amide.



■ INTRODUCTION

Carbon dioxide is an attractive C_1 feedstock as it is renewable, inexpensive, and can replace commonly used toxic C_1 building blocks, such as phosgene.[1] Synthetic procedures that utilize CO_2 as a carbon feedstock may offer viable alternative routes toward organic compounds that are currently derived from fossil fuel-based resources.[2] In this regard, an important transformation is the atom economical reaction of CO_2 with epoxides to yield cyclic carbonates[3] (Scheme 1, eq 1), which have important applications as polar aprotic solvents and electrolytes in lithium-ion batteries, and are useful monomers for the production of polycarbonates.[4] However, a central challenge common to all transformations employing CO_2 is overcoming its kinetic and thermodynamic stability.[1]

Scheme 1. A New Paradigm for Epoxide Activation



Herein we report the development and detailed mechanistic investigation of a novel and continuous flow catalytic system for this important transformation. Requiring only catalytic quantities of feedstock chemicals (bromine itself or a combination of *N*-bromosuccinimide (NBS) and benzoyl peroxide (BPO)) in DMF, the efficient conversion of epoxides and CO_2 to cyclic carbonates that we present here enjoys a wide substrate scope and represents a new paradigm for epoxide opening, which we propose occurs by electrophilic activation of the epoxide by the bromine cation and nucleophilic activation of CO_2 by an amide, in this case DMF (Scheme 1).

Homogeneous and heterogeneous catalysts for this transformation have been reported previously, including metal−salen complexes,[5] metal−oxides,[6] organic bases or ammonium and phosphonium salts,[7] *N*-heterocyclic carbenes,[8] alkali metal salts,[9] and ionic liquids.[10] We reasoned that a continuous flow approach would ameliorate many of the limitations observed in these systems, including, low conversion,[10a] catalyst deactivation over time,[5] high gas pressures and high reactor temperatures, which present significant safety considerations, particularly in large-scale batch reactions.

Continuous flow methods are enabling technologies for a wide range of chemical transformations,[11,12] including gas−liquid biphasic reactions.[13] Advantages that are enjoyed in flow, relative to batch, that are relevant to the present case include the following: (1) the high surface-to-volume ratio and enhanced mass transport, which significantly improve the reaction efficiency; (2) facile automation, secured reproducibility, improved safety and process reliability, which are easily achieved; (3) space and energy savings, given that a compact equipment footprint can provide very high output; (4) scaling-out accomplished simply by extension of product collection time; and (5) straightforward scaling-up using optimized reaction parameters developed in a bench-scale continuous device, as they can be transferred directly to large-scale production without the need for substantial further optimization, a feature that stands in contrast to the difficulties that can occur during scale-up from a small-scale batch process.

Received: July 31, 2013
Published: November 20, 2013

dx.doi.org/10.1021/ja4079094 | *J. Am. Chem. Soc.* 2013, 135, 18497−18501

RESULTS AND DISCUSSION

We constructed the continuous flow apparatus used in these investigations from commercially available components, as summarized in the diagram shown in Figure 1,[14] and the experimental procedure can be summarized as follows: After the system was brought to the appropriate pressure (100 psi CO_2) and temperature (120 °C), a solution of epoxide (**1a**−**j**) and catalyst in DMF was introduced by a Harvard Syringe Pump. The CO_2 stream was metered into the system using a mass flow controller. The gas and liquid streams met at a Y-mixer, and a 1:1 (v:v) liquid/gas slug flow stream was observed at the out port. The reaction occurred at elevated temperature in standard stainless steel tubing[15] (R1; 0.030 in. i.d.). Nitrogen (N_2) was employed for back pressure and a slow bleed was necessary to regulate the overall pressure of the system. After steady state was achieved (~4 × t_R where t_R is the residence time), the final eluent stream was sampled using a 6-way valve.[16]

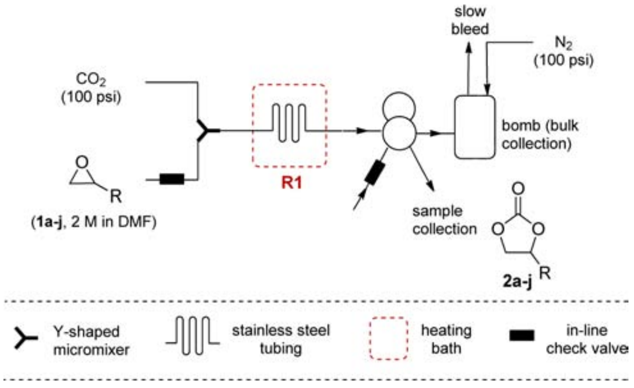
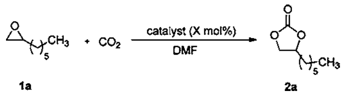


Figure 1. Schematic of gas−liquid continuous flow reactor.

In our initial studies of the reaction of CO_2 with epoxides (batch), we focused on the discovery of a catalyst system that (1) employed inexpensive and readily available compounds, (2) did not necessitate high CO_2 pressures, and (3) would be amenable to continuous flow production. During an evaluation of several classes of potential promoters, *N*-bromosuccinimide (NBS) emerged as an effective catalyst for the formation of cyclic carbonates from the corresponding epoxide and CO_2. For example, in the presence of 5 mol % of NBS in DMF, 75% conversion of 1,2-epoxyoctane (**1a**) to cyclic carbonate **2a** was observed after 6 h at 120 °C under batch conditions (Table 1, entry 1). Achieving a reasonable reaction time in flow (~45 min) was a significant challenge for this process, and initial continuous flow experiments were not promising. No conversion of 1,2-epoxyoctane (**1a**) was observed with 5 mol % of NBS at 80 °C, even with extending the t_R to 45 min (entry 2). Increasing the temperature to 120 °C gave only 24% conversion (entry 3). In contrast, the addition of benzoyl peroxide (BPO), to the continuous process resulted in 100% epoxide conversion under otherwise identical conditions (entry 4). Full epoxide conversion was also observed with decreased catalyst loading (5 mol %, entry 5). A solvent screen revealed that DMF, DMA, and NMP are appropriate solvents for the reaction.[17] DMF was selected for our study based on economic considerations. Further evaluation to decrease t_R and minimize the amount of solvent used revealed the optimal conditions to be 5 mol % of each of NBS and BPO, an epoxide concentration of 2.0 M in DMF, and a t_R of 30 min (entry 6).

Table 1. Initial Experiments Using the Continuous Flow Apparatus

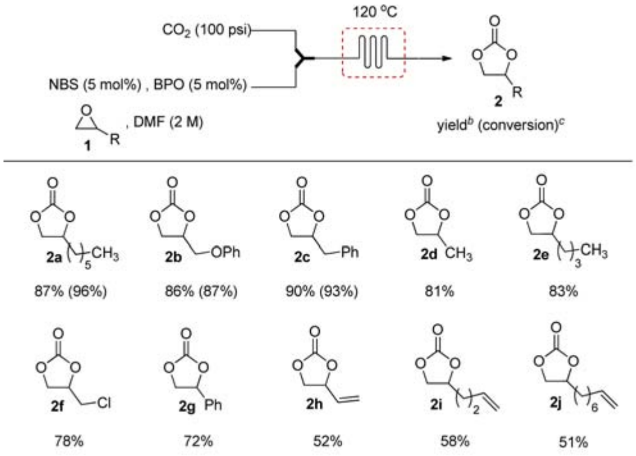


entry	catalyst (mol %)	*T* (°C)	time	[**1a**]$_0$ (M)	conv (%)[c]
1[a]	NBS (5)	120	6 h	0.44	75
2[b]	NBS (5)	80	45 min	1.0	0
3[b]	NBS (10)	120	45 min	1.0	24
4[b]	NBS/BPO (10/10)	120	45 min	1.0	100
5[b]	NBS/BPO (5/5)	120	45 min	0.44	100
6[b]	NBS/BPO (5/5)	120	30 min	2.0	96
7[b]	Br_2 (5)	120	7.8 min	0.5	50

[a] Batch reaction (atmospheric CO_2 pressure). [b] Flow experiment (100 psi CO_2 pressure). [c] Conversion determined by GC analysis using naphthalene as an internal standard.

Using the optimal conditions in the continuous flow apparatus (Table 1, entry 6), we investigated epoxides bearing different functional groups (Scheme 2). All terminal epoxides were converted to the corresponding cyclic carbonates in good to excellent yields with no observable byproduct formation (**2a**−**2g**). Propylene oxide (**1d**), a low boiling epoxide that can be difficult to handle, underwent smooth conversion to propylene carbonate (**2d**) in 81% yield. It should also be noted that the product, propylene carbonate (**2d**) is of high commercial value.[1] Alkene-containing epoxides were less than ideal substrates, forming cyclic carbonate products in only 52%, 58%, and 51% yield (**2h**−**2j**, respectively). We thus postulated that the pendant alkene interfered with the active catalyst in the reaction mixture (vide infra). However, while the reaction rate of **1i** was slower relative to that of epoxyoctane (**1a**), we did not observe any products in which the alkene had reacted (e.g., bromination).[18] Under the optimal conditions, disubstituted epoxides such as cyclohexene oxide, *trans*-stilbene oxide, and 1,1-dimethyloxirane were not converted to cyclic carbonates. Enantioenriched epoxides were evaluated and compared under

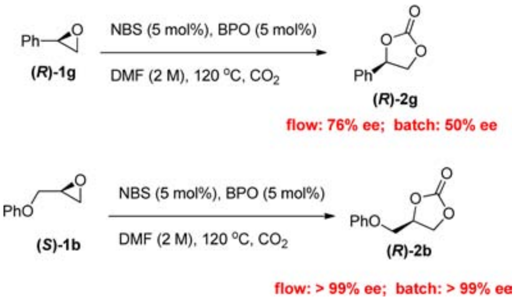
Scheme 2. Synthesis of Cyclic Carbonates from Epoxides and CO_2[a]



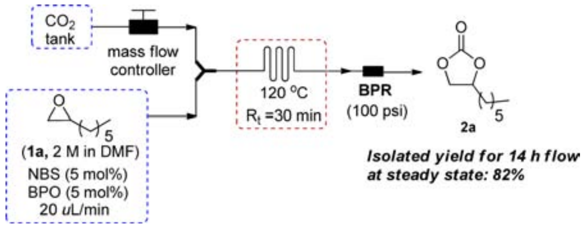
[a] See Table 1, entry 6 for experimental conditions. [b] Yield determined by ^{1}H NMR using trichloroethylene as an external standard. [c] Conversion (in parentheses) determined by GC analysis using naphthalene as an internal standard.

both flow and batch conditions (Scheme 3). Aliphatic substituted (*S*)-**1b** was converted to (*R*)-**2b** with no loss of ee. Enantiomerically pure aryl substituted (*R*)-**1g**, on the other hand, was transformed to (*R*)-**2g** with observable ee loss (76% ee) under flow conditions. Under batch conditions, product (*R*)-**2g** was achieved with an even lower selectivity (50% ee).[19] Use of a combination of a different pumping system (Syrris Asia) and a conventional, off-the-shelf back-pressure regulator is also possible, simplifying product collection and making laboratory use of this method even more straightforward (Scheme 4). In the case of epoxide **1a**, the system was operated at steady state for 14 h (28 residence times), and the results were very comparable to those of the other system: 92% conversion, 87% yield (NMR), 82% isolated yield after column chromatography.[18] Overall, the utility of the continuous flow reactor was demonstrated through the rapid synthesis of a variety of terminal cyclic carbonates with no observable byproducts.

Scheme 3. Transformations Using Enantioenriched Epoxides



Scheme 4. Simplified Flow Reactor



Mechanistic Investigations. The reaction conditions we discovered stand in stark contrast to those previously reported for this transformation; most of the components employed herein are generally considered electrophilic in nature, and it was unclear to us how two electrophilic catalysts (NBS and BPO) were mediating the coupling of two electrophiles (epoxide and CO_2). To gain mechanistic insight into this apparent paradox, we determined the kinetic parameters of the coupling of 1,2-epoxyoctane (**1a**) and CO_2 catalyzed by NBS and BPO in DMF.[18]

The rate of the reaction displayed a first-order dependence on the epoxide (Figure 2a,c), NBS (Figure 2b), and BPO concentrations (Figure 2d) and was *independent* of CO_2 pressure.[18,20] Notably, the reaction did not require BPO (Table 1, entries 1−3) yet was accelerated by it (entries 4 and 5). These results are easily explained by the following hypothesis: NBS catalysis involves two parallel pathways, one that does not require BPO (with a rate constant k_{10}^{exp}), and one that does (with a rate constant k_1^{exp}). These results can be collected to give the overall rate constant in terms of the *initial* NBS and BPO concentrations (see eq 2):

$$\frac{\mathrm{d[Epoxide]}}{\mathrm{d}t} = -(k_{10}^{\mathrm{exp}} + k_1^{\mathrm{exp}}[\mathrm{BPO}]_0)[\mathrm{NBS}]_0[\mathrm{Epoxide}\,] \tag{2}$$

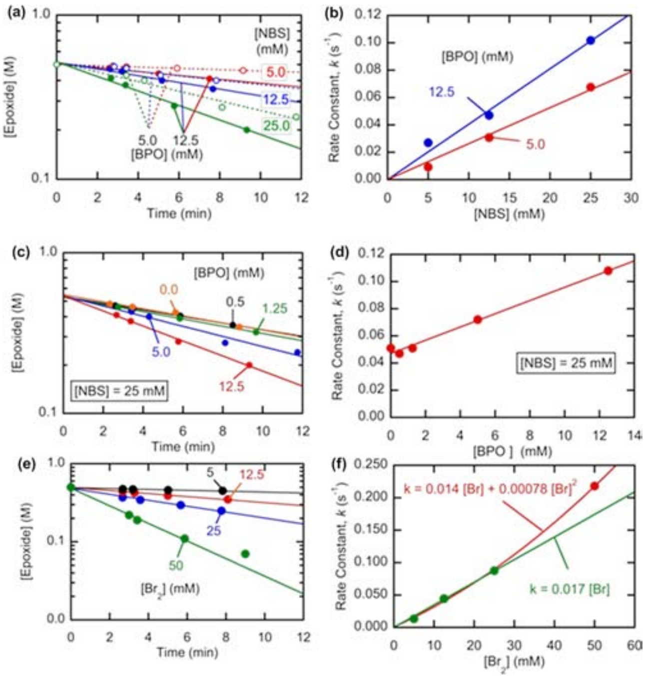
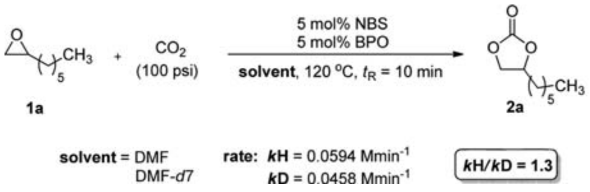


Figure 2. Selected kinetic experiment results showing effects of epoxides, NBS, BPO and Br_2 on epoxide coupling with CO_2.

Our solvent study[17] showed that DMF and DMA were critical for the reaction to achieve high conversion and yield, suggesting that the solvent may also be a direct promoter of the reaction. Indeed, the Parisi group has reported that *N*,*N*-dimethylamides can convert NBS to Br_2.[21] The Braddock group also demonstrated that DMF and DMA can behave as nucleophilic organocatalysts for the transfer of electrophilic bromine from NBS.[22] Moreover, highly enantioselective electrophilic brominations catalyzed by peptides, and Lewis base catalyzed alkene halofunctionalizations, were reported recently by Miller and Denmark, respectively.[23] On the other hand, CO_2 may be activated by DMF, as has been suggested by Aresta.[6a] We verified participation of DMF in the reaction mechanism by carrying out a solvent kinetic isotope effect (KIE) experiment. The relative rate of the reaction in DMF and DMF-d_7 (eq 3) was determined to be 1.3, suggesting a secondary KIE, such as a change of hybridization within DMF.

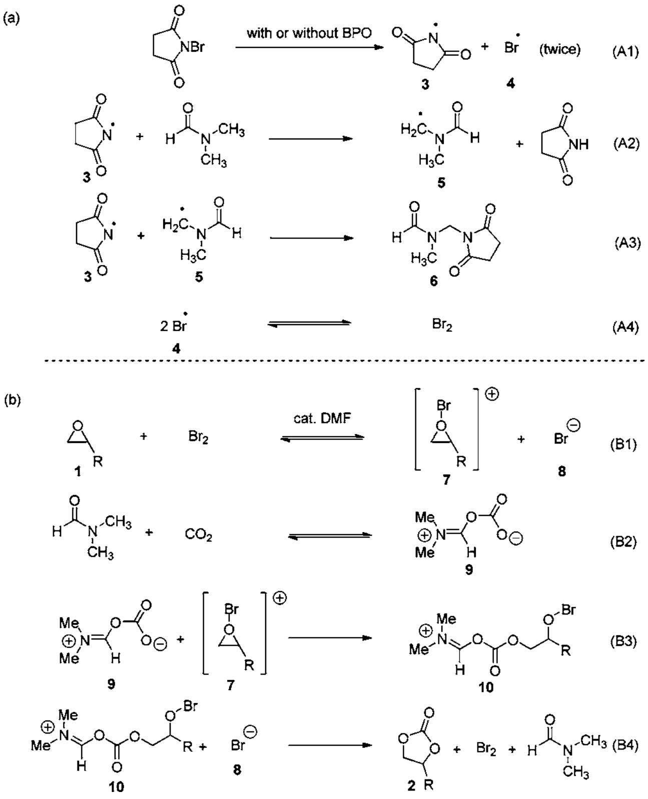


(3)

We suspected that the function of NBS and BPO was the generation of Br_2, which in turn may be the active catalyst, a supposition also consistent with the good performance of Br_2 in initial evaluations of preparative conditions (Table 1, entry 7).[24] A kinetic experimental study with pure bromine (in the absence of NBS and BPO) confirmed this notion (Figure 2e). The depletion of the epoxide with time was clearly dependent upon $[Br_2]$; the observed reaction rate constant is shown in Figure 2f to be essentially linear at low Br_2 concentrations, with a quadratic contribution at higher $[Br_2]$. The rate constants were similar in magnitude to those obtained when NBS was used as the catalyst, with BPO as a cocatalyst, strongly suggesting that Br_2 produced from NBS was the actual catalyst promoting the reaction.

On the basis of these results, we proposed a mechanism involving an in situ Br_2 generation (Scheme 5, eqs A1−A4) and a bromo-oxonium species (7).[25] Given the moderate nucleophilicity of the epoxide oxygen,[26] it is reasonable to propose the intermediacy of this cationic species **7** (eq B1). Moreover, bromine is known to react with other oxygen-containing compounds, such as ethers;[27] in fact, dioxane forms an isolable complex with elemental bromine.[28] Activated CO_2 **9** can react with **7** to give compound **10** (eq B3). It is also possible that bromide ion opens the bromo-oxonium species **7**, followed by activated CO_2 **9** displacement of bromide to give the same intermediate **10**. Epoxide opening at the less hindered (terminal) position was consistent with the observation that enantiomerically pure (*S*)-**1b** was converted to enantiomerically pure (*R*)-**2b** (retention of configuration, Scheme 3). The lower ee of (*R*)-**2g** was presumably due to increased stabilization of positive charge at the 2-position by the phenyl group. The regioselectivity of epoxide opening (with complete inversion of configuration of the minor regioisomer) would be one limiting scenario that would explain this result. It is also possible that the minor enantiomer is the result of an S_N1-like mechanism, followed by stereorandom attack of an activated CO_2 nucleophile (e.g., **9**, Scheme 5). After epoxide opening, the O−Br bond may be broken by bromide (Br^-), regenerating the Br_2 catalyst (eq B4) and liberating an alkoxide anion that undergoes cyclization to form the carbonate product.

Scheme 5. Proposed Mechanism



This kinetic model was further analyzed through mass balances on the reaction intermediates that were assumed to be at pseudo-steady state. The system of algebraic equations was solved for the unknown intermediate concentration [Br·] (see Supporting Information for details) that was further resolved into eq 4 by considering the homolysis/recombination of Br_2 to be reversible (note that all rate constants k_i are elementary in eq 4):

$$r_{\text{overall}} = \frac{k_4 k_{r4}[k_{10} + k_1[\text{BPO}]][\text{NBS}][\text{Epoxide}]}{2(k_4^2 - k_{r4}^2)} \quad (4)$$

This result is consistent with the experimentally determined rate expression given by eq 2. In the derived expression, the BPO concentration is constant due to its role as a cocatalyst. The NBS concentration is taken to be effectively constant due to the slow rate of Br_2 production relative to the kinetics of carbonate formation. It should be noted that the actual bromine concentration in the liquid phase may be significantly lower than the theoretical maximum because of partitioning of 65−95% of the Br_2 into the gas phase slug (largely CO_2). The exact amount will depend on the relative mass transfer rates between the two phases and Henry's Law constant (see Supporting Information for details).

■ CONCLUSION

A new method has been developed for the high yielding continuous synthesis of cyclic carbonates from CO_2 and epoxides. We have demonstrated how a continuous flow apparatus for gas/liquid reactions can greatly enhance the efficiency of the transformation relative to a traditional batch reactor. The catalysts used (NBS and BPO) are commercially available and inexpensive. A series of kinetics experiments supports epoxide activation by electrophilic bromine. Our laboratory is currently investigating other reactions involving CO_2 in which we can exploit this reactivity.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Design of flow reactor, experimental procedures, kinetics data, and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

tfj@mit.edu
tahatton@mit.edu

Author Contributions

§J.A.K. and J.W. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support for this work was provided by the DOE (DE-FOA-0000253) and the Siemens Corporation. We thank Dr. Christopher Smith and Prof. Klavs F. Jensen for help in the design of the continuous flow reactor, and Dr. Elena A. Arvanitis, Dr. Noorie Rajvanshi, and Dr. Amit Kapur from Siemens Corporation for helpful discussions.

REFERENCES

(1) (a) Aresta, M.; Dibenedetto, A. *Dalton Trans.* **2007**, 2975−2992. (b) Sakakura, T.; Choi, J. C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365. (c) North, M.; Pasquale, R.; Young, C. *Green Chem.* **2010**, *12*, 1514−1539.

(2) Illustrative examples of new conversions include: (a) Das Neves Gomes, C.; Jacquet, O.; Villiers, C.; Thuéry, P.; Ephritikhine, M.; Cantat, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 187. (b) Jacquet, O.; Das Neves Gomes, C.; Ephritikhine, M.; Cantat, T. *J. Am. Chem. Soc.* **2012**, *134*, 2934. (c) Yu, D.; Zhang, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20184.

(3) For selected reviews, see: (a) Darensbourg, D. J.; Mackiewicz, R. M.; Phelps, A. L.; Billodeaux, D. R. *Acc. Chem. Res.* **2004**, *37*, 836−844. (b) Decortes, A.; Castilla, A. M.; Kleij, A. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 9822−9837.

(4) Clements, J. H. *Ind. Eng. Chem. Res.* **2003**, *42*, 663−674.

(5) (a) North, M.; Pasquale, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 2946−2948. (b) Nroth, M.; Villuendas, P.; Young, C. *Chem.—Eur. J.* **2009**, *15*, 11454−11457.

(6) (a) Aresta, M.; Dibenedetto, A.; Gianfrate, L.; Pastore, C. *J. Mol. Catal. A: Chem.* **2003**, *204*−*205*, 245−252. (b) Yamaguchi, K.; Ebitani, K.; Yoshida, T.; Yoshida, H.; Kaneda, K. *J. Am. Chem. Soc.* **1999**, *121*, 4526−4527.

(7) (a) Caló, V.; Nacci, A.; Monopoli, A.; Fanizzi, A. *Org. Lett.* **2002**, *4*, 2561−2563. (b) Barbarini, A.; Maggi, R.; Mazzacani, A.; Mori, G.; Sartori, G.; Sartorio, R. *Tetrahedron Lett.* **2003**, *44*, 2931−2934. (c) Shen, Y.-M.; Duan, W.-L.; Shi, M. *Adv. Synth. Catal.* **2003**, *345*, 337−340. (d) Takahashi, T.; Watahiki, T.; Kitazume, S.; Yasuda, H.; Sakakura, T. *Chem. Commun.* **2006**, 1664−1666. (e) Tsutsumi, Y.; Yamakawa, K.; Yoshida, M.; Ema, T.; Sakai, T. *Org. Lett.* **2010**, *12*, 5728−5731.

(8) (a) Zhou, H.; Wang, Y.-M.; Zhang, W.-Z.; Qu, J.-P.; Lu, X.-B. *Green Chem.* **2011**, *13*, 644−650. (b) Zhou, H.; Zhang, W.-Z.; Liu, C.-H.; Qu, J.-P.; Lu, X.-B. *J. Org. Chem.* **2008**, *73*, 8039−8044.

(9) (a) Kihara, N.; Hara, N.; Endo, T. *J. Org. Chem.* **1993**, *58*, 6198−6202. (b) Jagtap, S. R.; Bhanushali, M. J.; Panda, A. G.; Bhanage, B. M. *Catal. Lett.* **2006**, *112*, 51−55. (c) Ramidi, P.; Munshi, P.; Gartia, Y.; Pulla, S.; Biris, A. S.; Paul, A.; Ghosh, A. *Chem. Phys. Lett.* **2011**, *512*, 273−277.

(10) (a) Udayakumar, S.; Park, S. W.; Park, D. W.; Choi, B. S. *Catal. Commun.* **2008**, *9*, 1563−1570. (b) Yang, Z.-Z.; Zhao, Y.-N.; He, L.-N. *RSC Adv.* **2011**, *1*, 545−567.

(11) Recent reviews on continuous-flow chemistry: (a) Anderson, N. G. *Org. Process Res. Dev.* **2012**, *16*, 852−869. (b) Webb, D.; Jamison, T. F. *Chem. Sci.* **2010**, *1*, 675−680. (c) Hartman, R. L.; Jensen, K. F. *Lab Chip* **2009**, *9*, 2495−2507. (d) Ley, S. V.; Baxendale, I. R. *Proc. of the Beilstein Symposium on Systems Chemistry, Bozen, Italy*, Eds. Hicks, M. and Kettner, C., 2009, 65−85.

(12) Recent reports from our laboratory: (a) Zhang, Y.; Blackman, M. L.; Leduc, A. B.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2013**, *52*, 4251−4255. (b) Kleinke, A. S.; Jamison, T. F. *Org. Lett.* **2013**, *15*, 710−713. (c) Shen, B.; Jamison, T. F. *Org. Lett.* **2012**, *14*, 3348−3351. (d) Sniady, A.; Bedore, M. W.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 2155−2158. (e) Palde, P. B.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 3525−3528.

(13) For recent reviews on characteristics of multiphase continuous reactions, see: (a) Günther, A.; Jensen, K. F. *Lab Chip* **2006**, *6*, 1487−1503. (b) Zhao, C.-X.; Middelberg, A. P. J. *Chem. Eng. Sci.* **2011**, *66*, 1394−1411. (c) Kashid, M. N.; Renken, A.; Kiwi-Minsker, L. *Chem. Eng. Sci.* **2011**, *66*, 3876−3897.

(14) See Supporting Information for full experimental details and a list of components.

(15) For an elegant and effective tube-in-tube reactor design for gas−liquid reactions: (a) O'Brien, M.; Taylor, N.; Polyzos, A.; Baxendale, I. R.; Ley, S. V. *Chem. Sci.* **2011**, *2*, 1250−1257. (b) Polyzos, A.; O'Brien, M.; Petersen, T. P.; Baxendale, I. R.; Ley, S. V. *Angew. Chem., Int. Ed.* **2011**, *50*, 1190−1193. Unfortunately, we were unable to use such reactors due to the permeability of CO_2 through both types of tubing at 120 °C.

(16) Another continuous flow example of this transformation, see ref 5b.

(17) Full details of solvent study can be found in the Supporting Information.

(18) See Supporting Information for details.

(19) For detailed ee analysis, see Supporting Information.

(20) At high BPO concentrations (>10 mol%), its rate dependence on BPO appeared to tend toward zeroth order.

(21) Caristi, C.; Cimino, G.; Feriazzo, A.; Gattuso, M.; Parisi, M. *Tetrahedron Lett.* **1983**, *24*, 2685−2688.

(22) Ahmad, S. M.; Braddock, D. C.; Cansell, G.; Hermitage, S. A. *Tetrahedron Lett.* **2007**, *48*, 915−918.

(23) (a) Gustafson, J. L.; Lim, D.; Miller, S. J. *Science* **2010**, *328*, 1251−1255. (b) Pathak, T. P.; Miller, S. J. *J. Am. Chem. Soc.* **2012**, *134*, 6120−6123. (c) Denmark, S. E.; Burk, M. T. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20655−20660. (d) Denmark, S. E.; Burk, M. T. *Org. Lett.* **2012**, *14*, 256−259.

(24) Even though Br_2 appeared to be an active catalyst for this transformation, we still utilized NBS/BPO system for our study due to its ease of handling and nontoxic properties.

(25) Sharghi, H.; Eskandari, M. M.; Ghavami, R. *J. Mol. Catal. A: Chem.* **2004**, *215*, 55−62.

(26) (a) Lambert, J. B.; Johnson, D. H. *J. Am. Chem. Soc.* **1968**, *90*, 1349−1350. (b) Wan, S.; Gunaydin, H.; Houk, K. N.; Floreancig, P. E. *J. Am. Chem. Soc.* **2007**, *129*, 7915−7923.

(27) (a) Pajeau, P. *Bull. Soc. Chim.* **1960**, 621. (b) Kratzl, K.; Schubert, K. *Monatsch. Chem.* **1950**, *81*, 988−995.

(28) Kosolapoff, G. M. *J. Am. Chem. Soc.* **1953**, *75*, 3596−3597.