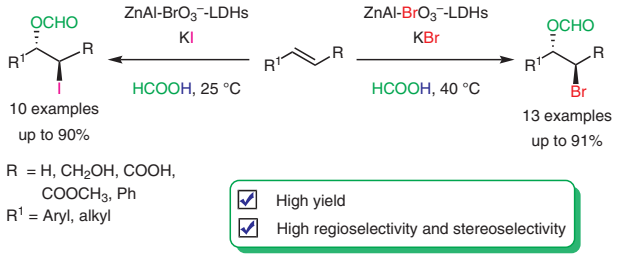
Synlett L. Wang et al. Letter

Green Synthesis of Haloformates from Olefins Using Formic Acid as Reactant, Protonic Acid, and Solvent

Ligeng Wang*
Hualong Zhang
Qin Yu
Chun Feng
Jun Hu*

College of Chemical Engineering, Zhejiang University of Technology, Zhejiang 310014, P. R. of China
wanglg@zjut.edu.cn
hjzjut@zjut.edu.cn



Received: 05.02.2018
Accepted after revision: 02.05.2018
Published online: 07.06.2018
DOI: 10.1055/s-0037-1610028; Art ID: st-2018-w0079-l

Abstract Bromoformates and iodoformates are successfully synthesized in high yields with regioselectivity and stereoselectivity by using ZnAl-BrO_3^- layered double hydroxides (LDHs) and KX (X = Br, I) in the presence of formic acid (HCOOH). The protocol exploits the versatile function of formic acid as solvent, nucleophilic reagent, and acidic medium simultaneously, simplifying the reaction and separation of the products.

Key words olefins, formic acid, bromoformates, iodoformates, regioselectivity, stereoselectivity

Halofunctionalization of olefins plays an important role in organic synthesis.[1] Compounds (halohydrins, β-haloesters) from this kind of reaction are prepared by adding halogen and a valuable nucleophilic reagent to the carbon–carbon double bond in a regioselective and stereoselective manner.[2] There are a number of vicinal halo-formyloxylated synthons as precursors for many vital compounds which can be applied to pharmaceuticals[3] and organic synthesis,[4] such as epoxides with high optical activity.[5] Moreover, halogen atoms can also be substituted by nucleophilic reagents to transform other significant compounds[6] through the S_N1 or S_N2 pathway.[7]

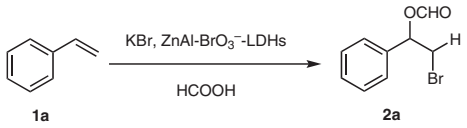
Chemists have increasingly paid attention to the vicinal halo-formyloxylation of carbon–carbon double bond, exploring many protocols which are focused on the variety of halogenating reagents. Only De Souza et al. reported the iodoformyloxylation of olefins employing TCCA, NBSac.[8] However, many other protocols based on bromoformyloxylation have constantly been put forward. For instance, NBS[9] and $TsNBr_2$[10] have been reported for performing simple and efficient bromoformyloxylation. Even though trouble-free strategies and user-friendliness should be the standard to follow during the design of a reaction,[11] the preparation of all these halogenating reagents inevitably involves liquid bromine and solid iodine. Therefore, scientists are actively engaged to explore nonpolluting and safer redox protocols. Recently, bromoformates were prepared by using NH_4Br and Oxone with excellent diastereoselectivity.[12] Subsequently, Chevella and co-workers synthesized iodoformates with NH_4I and Oxone in the presence of DMF.[13] Obviously, DMF is profoundly preferred by chemists because of its outstanding solubility as well as nucleophilicity, being widely applied to the type of reaction. Nonetheless, it is the intersolubility with H_2O and organic solvents in any proportion that cause the inefficient separation for organic products, which stimulates the further research for a synthetic method that is efficient, simple, and easy to handle.

Formic acid (HCOOH), known as the simplest organic carboxylic acid,[14] possesses the property of dissolving organic and mineral salts simultaneously. As the target products are fleetly separated from the reaction system, formic acid has been severed as reaction medium to promote organic synthetic transformations.[15] In the meanwhile, $HCOO^-$ dissociating from HCOOH has an ideal nucleophilicity for formyloxylation reactions.[16] Moreover, formic acid creates a moderately acidic environment in which highly active halogen sources generated from ZnAl-BrO_3^--LDHs[17]/KX (X = Br, I) react with substrates in situ.[18] Herein, we report a protocol of bromoformyloxylation and iodoformyloxylation of olefins using ZnAl-BrO_3^--LDHs and KX (X = Br, I) in the presence of formic acid, providing a large amount of bromide and iodine in a short time. In comparison with other protocols, this method is not only a more exciting approach slowly generating the halogen source in situ, but also provides a suitable chemical environment in which the full advantage of formic acid is taken with regard to acidity, solubility, nucleophilicity.

The bromoformyloxylation reaction was initially studied by using styrene as a model substrate in the presence of ZnAl-BrO_3^--LDHs [1.0×10^{-3} mol (BrO_3^-)/g (ZnAl-BrO_3^--LDHs)],[17] KBr, HCOOH, and the outcome of the reaction was investigated under different conditions by varying the temperature and volume of solvent. The corresponding results are illustrated in Table 1. Apparently, styrene only provided the bromoformyloxylation product in 53% yield at 25 °C, with use of 10 mL of formic acid (entry 1). Moreover, nearly half of the by-product was dibromination product, which was determined by NMR spectroscopy. Because of the almost equal nucleophilicity of $HCOO^-$ and Br^-at relatively low temperature, the system accessed the competitive nucleophilic reaction and produced dibromination and bromoformyloxylation products with the same probability. Yields markedly improved as the temperature increased. Importantly, styrene could afford the corresponding product in 90% at 40 °C (entry 3) because then the nucleophilicity of $HCOO^-$ absolutely surpassed that of Br^- according to our hypothesis. On the contrary, yields decreased by elevating the temperature and the product was obtained in 85% at 45 °C and in 69% at 50 °C (entries 4–5). It is a small amount of H_2O that is produced from the interaction between HCOOH and ZnAl-BrO_3^--LDHs for BrO_3^-, which acts as a kind of nucleophilic reagent to compete with other nucleophilic species, such as $HCOO^-$ and Br^-, which directly generates bromohydrins.[19] Similarly, the results indicate that the yields decreased with decreasing volume of solvent and the products were obtained in 86% with 8 mL and in 73% with 6 mL of solvent (entries 6–7). Probably the denseness of the reaction mixture, which increased as the volume of solvent decreased in the biphasic formic acid–hydrotalcite mixture, prevented a proper homogeneity of the reaction. Furthermore, the reduction of the volume of formic acid from 10 to 6 mL directly led to the decline of acidity and concentration of $HCOO^-$ in the whole solution, which ultimately impacted the nucleophilicity of $HCOO^-$ and the redox reaction between BrO_3^- and Br^-. Consequently, the reaction conditions were eventually settled as 0.4 equivalents BrO_3^- (calculated according to the content of BrO_3^- intercalated in ZnAl-BrO_3^--LDHs), 0.8 equivalents KBr, 10 mL of formic acid, at 40 °C.

A series of diverse derivatives were selected for exploring the scope and generality of the bromoformyloxylation process with the optimized reaction conditions established from Table 1, and the results are shown in Scheme 1. Because alkyl and aryl groups activate the benzene ring, the reactivity of the double bond at the *para* position increases in a way. 2-Ethenylnaphthalene and 4-*tert*-butylstyrene having an electron-donating group on the benzene ring easily afforded the corresponding bromoformate products 2-bromo-1-(4-*tert*-butylphenyl)ethyl formate and 2-bromo-1-(naphthalen-2-yl)ethyl formate in 89 and 88% yield, respectively (**2b**, **2c**).

Table 1 Screening and Optimization of Bromoformyloxylation[a]



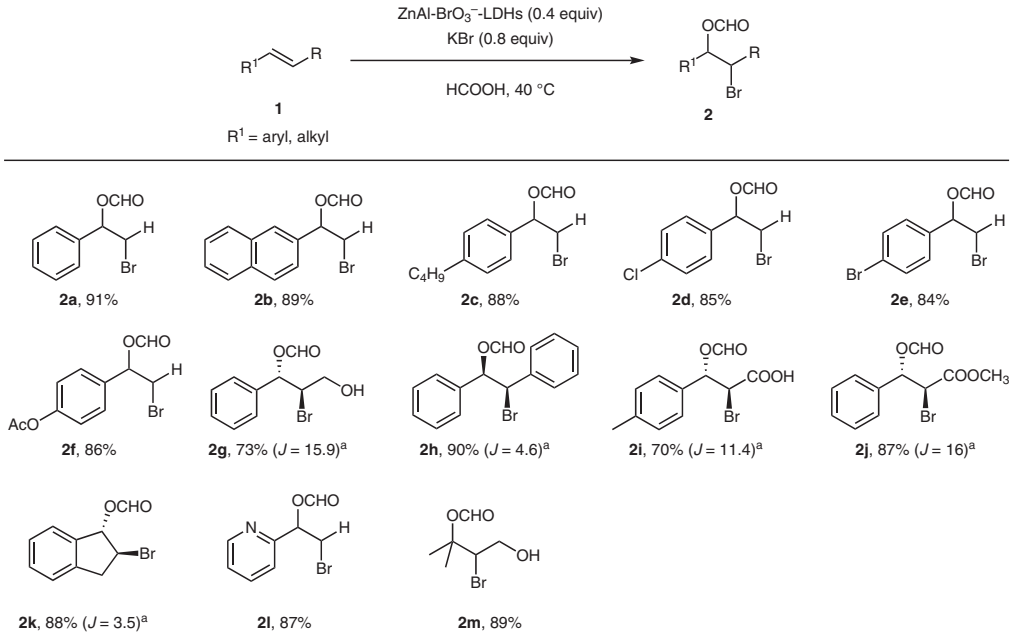
1a **2a**

Entry	Temp (°C)	HCO_2H (mL)	Yield (%)[b]
1	25	10	53
2	35	10	77
3	40	10	90
4	45	10	85
5	50	10	69
6	40	8	86
7	40	6	73

[a] *Reaction conditions*: styrene (**1a**) (2 mmol), ZnAl-BrO_3^--LDHs (0.8 g), KBr (1.6 mmol).
[b] Isolated yields after column chromatography.

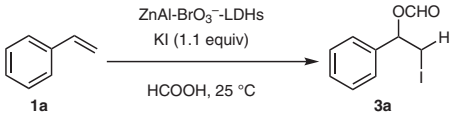
4-Chlorostyrene, 4-bromostyrene, 4-acetoxystyrene bearing electron-withdrawing groups with inductive effect reacted smoothly, yielding the corresponding vicinal bromoformates in similar yields (**2d–f**). Moreover, olefin derivatives with substituents at the β-position of terminal styrene were investigated. Unsatisfyingly, cinnamyl alcohol gave the corresponding *erythro*-bromoformate product in only 73% yield (**2g**) along with obvious by-product. However, *cis*-stilbene gave the *threo*-bromoformate product in 90% yield (**2h**). α,β-Unsaturated olefins, such as 4-methycinnamic acid and methyl *trans*-cinnamate, performed well to afford the desired *erythro*-bromoformate products (**2i**, **2j**). Similarly, the reaction of indene also achieved the *trans*-addition product in 88% yield (**2k**). Furthermore, 2-ethenylpyridine and 3-methy-2-buten-1-ol furnished the desired bromoformate in 87 and 89% yield (**2l**, **2m**), which primely proved that the protocol can be applied to olefins bearing a heterocyclic ring and simple alkenes.

Encouraged by the results of this vicinal bromoformyloxylation, we also considered iodoformyloxylation of olefins under similar reaction conditions, because iodinated organic compounds have significant applications. The iodoformyloxylation reaction was investigated by varying the mass of ZnAl-BrO_3^--LDHs with styrene being selected as a model substrate at 25 °C, and the results are summarized in Table 2. The iodoformyloxylation product of styrene was obtained in only 38% yield (entry 1) with use of 0.35 g ZnAl-BrO_3^--LDHs which is the minimum mass when I^- is oxidized to I_2 in an acidic environment.



Scheme 1 *Reaction conditions*: substrate **1** (2 mmol), ZnAl-BrO_3^--LDHs (0.8 g), KBr (1.6 mmol). Isolated yields after column chromatography. [a] *J* is the coupling constant value of protons attached to the carbons bearing –OCHO and Br groups and was determined by ^{1}H NMR spectroscopy.

Table 2 Screening and Optimization of Iodoformyloxylation[a]



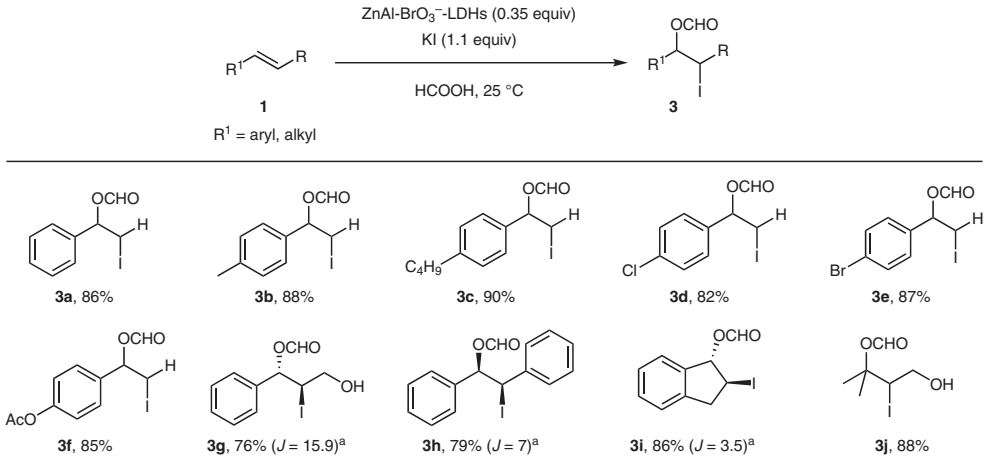
Entry	ZnAl-BrO_3^--LDHs (g)	Yield (%)[b]
1	0.35	30
2	0.45	59
3	0.55	64
4	0.65	78
5	0.70	86
6	0.75	86
7	0.80	85

[a] *Reaction conditions*: styrene (**1a**) (2 mmol), KI (2.2 mmol), HCO_2H (10 mL).
[b] Isolated yields after column chromatography.

Moreover, the yields increased as the mass of ZnAl-BrO_3^--LDHs was increased, attaining 59, 64 and 78% (entries 3–4). Essentially, the yields continuously increased as the degree of oxidation that represents the content of I^+ decreased. Markedly, 0.7 g ZnAl-BrO_3^--LDHs (the minimum mass when I^- is oxidized to I^+ in acidic medium) gave the highest yield of 86% (entry 5). Apparently, yields tended to be stable when the mass of ZnAl-BrO_3^--LDHs exceeded 0.7 g (entries 6–7). Therefore, we assumed that olefins reacted with iodine based on I^- being oxidized to I^+ by BrO_3^- intercalated in the hydrotalcite. Consequently, to evaluate the scope of this reaction system, optimal reaction conditions were selected as 0.35 equivalents BrO_3^-, 1.1 equivalents KI, 10 mL of formic acid, at 25 °C.

The protocol was examined for a range of styrene derivatives and the results are shown in Scheme 2. The styrene derivatives with electron-donating groups, such as methyl and *tert*-butyl provided corresponding iodoformates in 88 and 90% yield (**3b**, **3c**). In the meantime, 4-chlorostyrene, 4-bromostyrene, and 4-acetoxystyrene, which bear electron-withdrawing groups on the benzene ring, achieved the products in 82, 87 and 85% yield, respectively (**3d–f**). In addition, olefin derivatives with substituents at the β-position of terminal styrene also attained the corresponding iodoformates. Cinnamyl alcohol successfully gave the desired *erythro*-iodoformate product in 76% yield (**3g**) and *cis*-stilbene provided the *threo*-iodoformate product in 79% yield (**3h**). Indene classified as an internal aromatic olefin was compatible with these reaction conditions, and the corresponding product was obtained in 86% yield (**3i**).

The coupling constant (*J*) values of the two protons attached to the adjacent carbon atoms mainly depend on the dihedral angle of the two protons in the ^{1}H NMR spectrum, being calculated by the Karplus empirical formula (based on experimental data): $J = A + B \cos \Phi + C \cos 2\Phi$ (A = 7, B = –1, C = 5). Generally, the coupling constant *J* is greater than 8 Hz when the dihedral angle is 0/180°. In the meantime, the coupling constant *J* is less than 7 at 60°. Therefore, after stereoselective bromoformyloxylation and iodoformyloxyaltion of 1,2-disubsituted olefins, the coupling constant *J* of protons attached to the carbons bearing –OCHO and Br/I

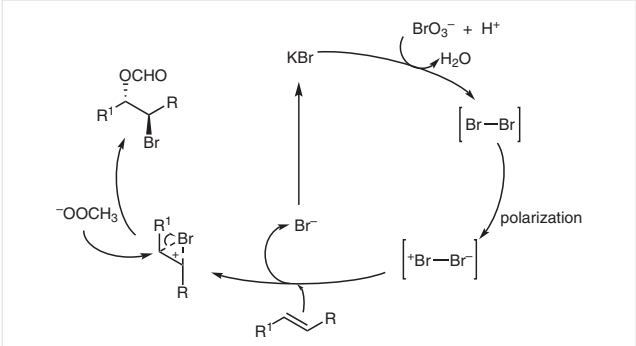


Scheme 2 *Reaction conditions*: substrate **1** (2 mmol), ZnAl-BrO_3^--LDHs (0.7 g), KI (2.2 mmol). Isolated yields after column chromatography. [a] *J* is the coupling constant value of protons attached to the carbons bearing –OCHO and I groups and was determined by ^{1}H NMR spectroscopy.

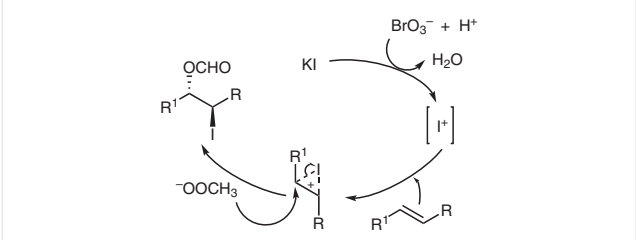
groups in the ^{1}H NMR spectrum can prove that the bromoformyloxylation and iodoformyloxyaltion predominately follow *anti* addition, which indirectly testifies that the reactions proceed via a bromonium-ion or an iodonium-ion intermediate. Furthermore, the difference in electronegativity between –OCHO and Br/I directly causes the distinction of the chemical shift (δ) values of the protons. In the regioselective bromoformyloxylation and iodoformyloxyaltion, it can be certified that the –OCHO attaches to the α -position (benzyl) and the Br/I locates at the β-position.

After the formation of the bromonium-ion or iodonium-ion intermediate, a stable benzylic cation, which presents a higher partial positive charge in α-position, is formed. Consequently, the α-position is much more easily attacked by $HCOO^-$ than the β-position, leading, therefore, to high regioselectivity.

Scheme 3 shows a plausible mechanism which can explain the synthetic process of bromoformyloxylation with regioselectivity and stereoselectivity. It is confirmed that BrO_3^- released from ZnAl-BrO_3^--LDHs in acid medium reacts with KBr to generate the bromine source in the transient state of Br–Br.[20] Immediately, Br–Br undergoes polarization to the shape of Br^+–Br^- in strongly polar solvent. The Br^+–Br^- species then reacts with a C=C double bond in situ, forming a three-membered cyclic bromonium-ion intermediate[21] and Br^- that can recycle after redox reaction with BrO_3^-. Owing to the hard electrophilicity of the α-position, formate as a kind of nucleophilic species attacks the α-position from the *anti* side through the S_N2 pathway. Subsequently, the three-membered ring is opened and the product of bromoformyloxylation is obtained from the bromonium-ion intermediate simultaneously. A probable mechanistic pathway for explaining the iodoformyloxylation is shown in Scheme 4. What is different from the mechanism of bromoformyloxylation is that I^- is directly oxidized to I^+ species by BrO_3^-.



Scheme 3 Proposed mechanism for bromoformyloxylation



Scheme 4 Proposed mechanism for iodoformyloxylation

In conclusion, a new protocol for high-yielding bromoformyloxylation[22] and iodoformyloxylation of olefins using ZnAl-BrO_3^--LDHs and KX (X = Br, I) in the presence of formic acid has been reported and is provided with universal adaptability for different types of substrates. It is noteworthy that the bromoformyloxylation and iodoformyloxyl-

ation products exhibit excellent regioselectivity and stereoselectivity. The new manner of providing a halogen source instead of using halogenating agents is in accordance with the green chemical idea for inexpensive, flexible operation, atom economy, and non-pollution. The concept reflected in this study is that a kind of formic acid reagent has multiple functions, which greatly simplifies the reaction and separation of the products.

Acknowledgment

The center of forecasting and analysis in Zhejiang University of Technology is greatly appreciated. We thank Qingbao Song and Aimin Chen for suggestions in this paper.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610028.

References and Notes

(1) (a) Dewkar, G. K.; Narina, S. V.; Sudalai, A. *Org. Lett.* **2003**, *5*, 4501. (b) Damin, B.; Garapon, J.; Sillion, B. *Synthesis* **1981**, 362. (c) Damin, B.; Garapon, J.; Sillion, B. *Tetrahedron Lett.* **1980**, *21*, 1709.

(2) (a) Macharla, A. K.; Nappunni, R. C.; Nama, N. *Tetrahedron Lett.* **2012**, *53*, 1401. (b) Phukan, P.; Chakraborty, P.; Kataki, D. J. *J. Org. Chem.* **2006**, *71*, 7533. (c) Taber, D. F.; Liang, J. L. *J. Org. Chem.* **2007**, *72*, 431. (d) Yeung, Y. Y.; Gao, X.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 9644.

(3) (a) Tripathy, N. k. *Georg G. I.* **2004**, *45*, 5309. (b) Buynak, J. D.; Mathew, J.; Rao, M. N. *J. Chem. Soc., Chem. Commun.* **1986**, *12*, 941. (c) Thiem, J.; Gerken, M. J. *Carbohydr. Chem.* **1982**, *1*, 229. (d) Liang, J.; Moher, E. D.; Moore, R. E.; Hoard, D. W. *J. Org. Chem.* **2000**, *65*, 3143.

(4) (a) Anderson, J. C.; Headley, C.; Stapleton, P. D.; Taylor, P. W. *Tetrahedron* **2005**, *61*, 7703. (b) Li, L.; Chan, T. H. *Org. Lett.* **2001**, *3*, 739. (c) Larivée, A.; Unger, J. B.; Thomas, M.; Wirtz, C.; Dubost, C.; Handa, S.; Fürstner, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 304.

(5) Kolb, H. C.; Sharpless, K. B. *Tetrahedron* **1992**, *48*, 10515.

(6) (a) Hamm, S.; Henning, L.; Findeisen, M.; Müller, D.; Welzel, P. *Tetrahedron* **2000**, *56*, 1345. (b) Suginome, H.; Wang, J. B. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 193.

(7) (a) Glukhovtsev, M. N.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1995**, *117*, 9012. (b) Xiao, M. Y.; Ren, D. D.; Xu, L. B.; Li, S. S.; Yu, L. P.; Xiao, J. *Org. Lett.* **2017**, *19*, 5724. (c) Ortiz, R.; Herrera, R. P. *Molecules* **2017**, *22*, 574. (d) Zhu, Y.; Mei, H. B.; Han, J. L.; Soloshonok, V. A.; Zhou, J.; Pan, Y. *J. Org. Chem.* **2017**, *82*, 13663. (e) Miralles, N.; Gomez, J. E.; Kleij, A. W.; Fernandez, E. *Org. Lett.* **2017**, *19*, 6096.

(8) De Souza, A. V. A.; Mendonca, G. F.; Bernini, R. B.; De Mattos, M. C. S. *J. Braz. Chem. Soc.* **2007**, *18*, 1575.

(9) Dalton, D. R.; Smith, R. C. J.; Jones, D. G. *Tetrahedron* **1970**, *26*, 575.

(10) Saikia, I.; Krishna, K. R.; Phukan, P. *Tetrahedron Lett.* **2012**, *53*, 758.

(11) Podgoršek, A.; Eissen, M.; Fleckenstein, J.; Stavber, S.; Zupan, M.; Iskra, J. *Green Chem.* **2009**, *11*, 120.

(12) Mameda, N.; Peraka, S.; Macharla, A. K.; Marri, M. R.; Kodumuri, S.; Nama, N. *Tetrahedron Lett.* **2014**, *55*, 3926.

(13) Chevella, D.; Mameda, N.; Macharla, A. K.; Peraka, S.; Marri, M. R.; Kodumuri, S.; Nama, N. *Synth. Commun.* **2016**, *13*, 1133.

(14) (a) Niizato, H.; Ueno, Y.; Takemura, S. *Chem. Pharm. Bull.* **1972**, *20*, 2707. (b) Ueno, Y.; Yamasaki, A.; Terauchi, H.; Takemura, S. *Chem. Pharm. Bull.* **1974**, *22*, 1646.

(15) (a) Ganboa, I.; Palomo, C. *Synth. Commun.* **1983**, *13*, 941. (b) Li, X. K.; Ho, B.; Lim, D. S. W.; Zhang, Y. G. *Green Chem.* **2017**, *19*, 914. (c) Zhang, F.; Lu, Q.; Yue, X. X.; Zuo, B. Q.; Qin, M. D.; Li, F.; Kaplan, D. L.; Zhang, X. G. *Acta Biomater.* **2015**, *12*, 139. (d) Schettini, A. R. A.; Peres, R. C. D.; Soares, B. G. *Synth. Met.* **2009**, *159*, 1491. (e) Schueren, L. V. D.; Steyaert, I.; Schoenmaker, B. D.; Clerck, K. D. *Carbohydr. Polym.* **2012**, *88*, 1221.

(16) (a) Kozar, L. G.; Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1977**, *42*, 1386. (b) Kleinfelter, D. C.; Schleyer, P. v. R. *Org. Synth.* **1962**, *42*, 79. (c) Kaulen, J. *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 773. (d) Wang, L.; Floreancig, P. E. *Org. Lett.* **2004**, *6*, 4207.

(17) (a) Wang, L. G.; Zheng, F. X.; Jiang, C. X.; Ni, Z. M. *J. Chin. Ceram. Soc.* **2015**, *43*, 672. (b) Yang, M. S.; Gu, L. H.; Yang, B.; Wang, L.; Sun, Z. Y.; Zheng, J. Y. *Appl. Surf. Sci.* **2017**, *426*, 185. (c) Djebbi, M. A.; Elabed, A.; Bouaziz, Z.; Sadiki, M.; Elabed, S.; Namour, P.; Jaffrezic-Renault, N.; Amare, A. B. H. *Int. J. Pharm.* **2016**, *515*, 422.

(18) (a) Veeraiah, T.; Sondu, S. *Int. J. Chem. Sci.* **2007**, *5*, 911. (b) Imbri, D.; Netz, N.; Kucukdisli, M.; Kammer, L. M.; Jung, P.; Kretzschmann, A.; Opatz, T. *J. Org. Chem.* **2014**, *79*, 11750. (c) Karama, U.; Mahfouz, R.; Al-Othman, Z.; Warad, I.; Almansour, A. *Synth. Commun.* **2013**, *43*, 893. (d) Solladié, N.; Gross, M. *Tetrahedron Lett.* **1999**, *40*, 3359.

(19) (a) Song, S.; Huang, X. Q.; Liang, Y. F.; Tang, C. H.; Li, X. W.; Jiao, N. *Green Chem.* **2015**, *17*, 2727. (b) Dong, J. J.; Fernández-Fueyo, E.; Li, J. B.; Guo, Z.; Renirie, R.; Wever, R.; Hollmann, F. *Green Chem.* **2017**, *53*, 6207. (c) Lodh, R. S.; Borah, A. J.; Phukan, P. *Indian. J. Chem.* **2014**, 53B, 1425.

(20) (a) Adimurthy, S.; Ghosh, S.; Patoliya, P. U.; Ramachandraiah, G.; Agrawal, M.; Gandhi, M. R.; Upadhyay, S. C.; Ghosh, P. K.; Ranu, B. C. *Green Chem.* **2008**, *10*, 232. (b) Cortes, C. E. S.; Faria, R. B. *Inorg. Chem.* **2004**, *43*, 1395.

(21) (a) Zheng, C. Y.; Slebocka-Tilk, H.; Nagoraski, R. W.; Alvarado, L.; Brown, R. S. *J. Org. Chem.* **1993**, *58*, 2122. (b) Heasley, V. L.; Shellhamer, D. F.; Iskilian, J. A.; Street, D. L. *J. Org. Chem.* **1978**, *43*, 3139. (c) Vardhan, H. B.; Bach, R. D. *J. Org. Chem.* **1992**, *57*, 4948. (d) Slebocka-Tilk, H.; Nagorski, S. M. R. W.; Brown, P. T. R. S.; McDonald, R. *J. Am. Chem. Soc.* **1995**, *117*, 8769. (e) Chiappe, C.; Rubertis, A. D.; Jaber, A.; Lenoir, D.; Wattenbach, C.; Pomelli, C. S. *J. Org. Chem.* **2002**, *67*, 7066. (f) McClendon, E.; Omollo, A. O.; Valente, E. J.; Hamme, A. T. *Tetrahedron Lett.* **2009**, *50*, 533.

(22) **Representative Procedure for the Synthesis of Bromoformate 2f**

Substrate (**1f**, 324.4 mg, 2 mmol), KBr (190.4 mg, 1.6 mmol), formic acid (10 mL) were added to a 50 mL three-necked flask, and KBr was absolutely dissolved in the mixture with proper stirring at room temperature. After ZnAl-BrO_3^--LDHs (0.8 g) was added to the mixture, the reaction system was stirred at 40 °C with use of a reflux condenser in a water bath until the substrate completely disappeared (monitored by TLC). The molecular bromine was treated with sodium bisulfite solution right away. The solid phase ZnAl-BrO_3^--LDHs was removed by centrifugation. Furthermore, the dichloromethane (3 × 5 mL) used for washing the ZnAl-BrO_3^--LDHs was merged into the liquid mixture after centrifugation. Then, the products were extracted

into the organic phase with dichloromethane (3 × 10 mL) and H_2O (30 mL). The organic phase was dried with sodium sulfate and concentrated in vacuum. The crude product was purified by column chromatography on silica gel.

2-Bromo-1-(4-acetoxylphenyl)ethyl formate (2f)

Yield: 493.8 mg, 86%. Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.42–7.39 (m, 2 H), 7.14–7.12 (m, 2 H), 6.11 (dd, *J* = 8.3, 4.5 Hz, 1 H), 3.68 (dd, *J* = 11.0, 8.4 Hz, 1 H), 3.61 (dd, *J* = 11.0, 4.5 Hz, 1 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 169.16, 159.52, 151.09, 134.49, 127.84, 122.00, 74.04, 33.51, 21.07 ppm. HRMS (ESI): *m*/*z* calcd for $C_{11}H_{11}BrO_4$ $[M + H]^+$: 286.9919; found: 286.9917.