

Calcium L-Lactate Frameworks as Naturally Degradable Carriers for Pesticides

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S Supporting Information

ABSTRACT: Two porous, chiral metal–organic frameworks (MOFs), $\text{Ca}_{14}(\text{L-lactate})_{20}(\text{acetate})_8(\text{C}_2\text{H}_5\text{OH})(\text{H}_2\text{O})$ (MOF-1201) and $\text{Ca}_6(\text{L-lactate})_3(\text{acetate})_9(\text{H}_2\text{O})$ (MOF-1203), are constructed from Ca^{2+} ions and L-lactate [$\text{CH}_3\text{CH}(\text{OH})\text{COO}^-$], where Ca^{2+} ions are bridged by the carboxylate and hydroxyl groups of lactate and the carboxylate group of acetate to give a three-dimensional arrangement of $\text{Ca}(-\text{COO}, -\text{OH})$ polyhedra supporting one-dimensional pores with apertures and internal diameters of 7.8 and 9.6 Å (MOF-1201) and 4.6 and 5.6 Å (MOF-1203), respectively. These MOFs represent the first examples of extended porous structures based on Ca^{2+} and lactate. They show permanent porosity of 430 and 160 $\text{m}^2 \text{g}^{-1}$, respectively, and can encapsulate an agriculturally important fumigant, *cis*-1,3-dichloropropene. MOF-1201 shows a 100 times lower release rate compared with liquid *cis*-1,3-dichloropropene under the same test conditions (25 °C, air flow rate of 1 $\text{cm}^3 \text{min}^{-1}$). The hydrolysis of MOF-1201 in water makes it the first example of a degradable porous solid carrier for such fumigants.

Metal–organic frameworks (MOFs) are porous crystalline materials constructed by linking metal ions with organic linkers.¹ The size, geometry, and functionality of the organic units and the variability of the metal ions have led to the discovery of more than 20 000 MOFs² with a wide range of applications in gas separation, storage, and catalysis.³ However, the majority of MOFs reported to date are based on transition metal ions and organic linkers derived from petrochemical sources, and their toxicity has precluded many of important applications requiring eco-friendly (environmentally friendly) materials, such as applications in the food industry, biomedicine, and agriculture.⁴

Preparation of MOFs from eco-friendly metal ions such as Ca^{2+} and nontoxic, naturally occurring linkers would expand the scope of applications.^{4,5} However, their synthesis remains a challenge, and there have been no reported examples of such Ca^{2+} -based MOFs as porous materials. This challenge is due to the multiplicity of coordination geometries and high coordination number of Ca^{2+} ions and the flexibility of naturally occurring organic linkers, thus resulting in dense, nonporous structures.^{4,6}

Herein we report the synthesis of two MOFs based on Ca^{2+} ions and naturally occurring lactate and acetate linkers, $\text{Ca}_{14}(\text{L-lactate})_{20}(\text{acetate})_8(\text{C}_2\text{H}_5\text{OH})(\text{H}_2\text{O})$ (MOF-1201) and $\text{Ca}_6(\text{L-lactate})_3(\text{acetate})_9(\text{H}_2\text{O})$ (MOF-1203).⁷ We demonstrate their permanent porosity and the potential of using MOF-1201 as a carrier for the slow release of the fumigant *cis*-1,3-dichloropropene. The disassembly of this MOF in water makes it the first example of a degradable porous carrier for delivery of fumigants.

Hydrothermal reaction of a suspension of calcium acetate and L-lactic acid in ethanol (methanol) at 120 °C (100 °C) for a period of 4 (3) days gave colorless rod-shaped crystals of MOF-1201 (needle-shaped crystals of MOF-1203). The crystals were then harvested for single-crystal X-ray diffraction (SCXRD) analysis. The exact molar ratios of the lactate and acetate linkers in the MOFs were further determined by ¹H NMR spectroscopy and elemental microanalysis of the solvent-free samples (see section S1 in the Supporting Information).

SCXRD analysis revealed that both MOF-1201 and MOF-1203 are extended frameworks constructed from Ca^{2+} as nodes and both lactate and acetate as linkers. MOF-1201 crystallizes in the monoclinic space group $P2_1$ with lattice constants $a = 24.39$ Å, $b = 13.26$ Å, $c = 24.97$ Å, and $\beta = 90.33^\circ$. In this structure, 14 crystallographically unique calcium atoms exist [Ca(1) to Ca(14)] (Figure 1a,c), all of which are capped by O atoms from lactate (carboxylic O or hydroxyl O), acetate (carboxylic O), or water to form calcium oxide polyhedra. The coordination modes of the linkers to Ca^{2+} vary—four different modes are found in lactate [(i), (ii), (iii), and (vi)] and three in acetate [(vii), (ix), and (xi)] (Figure 1c), among which the lactate with mode (vi) and the acetate with mode (vii) act as terminal ligands and cap only one Ca^{2+} center [Ca(5) and Ca(11), respectively], while the remaining others act as bridges to connect two or three Ca^{2+} . These bridging lactates and acetates link together all of the Ca^{2+} centers to form MOF-1201. For example, Ca(1), Ca(2), and Ca(3) are bridged by a lactate with coordination mode (i), with Ca(1) coordinated to the hydroxyl O and the adjacent carboxylic O, Ca(2) to only the carboxylic O, and Ca(3) to the other carboxylic O. Similarly, Ca(1), Ca(2), and Ca(4) are bridged by mode (i); Ca(4), Ca(5), and Ca(7) by mode (iii); Ca(7), Ca(8), and Ca(9) by mode (i); Ca(7), Ca(8), and Ca(10) by mode (i); Ca(10), Ca(11), and Ca(12) by mode (xi); Ca(6), Ca(5), and Ca(7) by mode (ii); and Ca(12), Ca(13), and Ca(14) by mode (i) to connect all of the Ca^{2+} centers (Figure S1).

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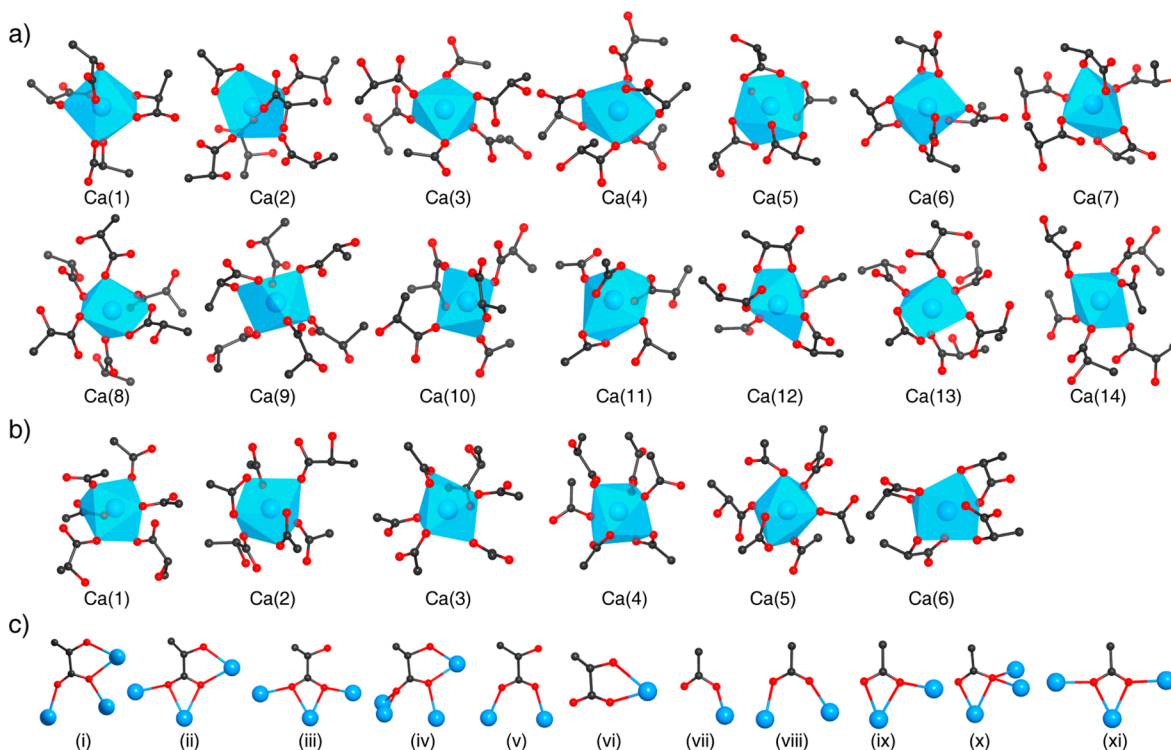


Figure 1. (a, b) Ca²⁺ centers in (a) MOF-1201 and (b) MOF-1203 and their coordination with lactate and acetate. The coordination numbers for Ca(1) to Ca(14) in MOF-1201 are 8, 7, 6, 7, 9, 8, 7, 7, 7, 7, 8, 7, 7, and 6, respectively. The coordination numbers for Ca(1) to Ca(6) in MOF-1203 are 7, 8, 7, 8, 7, and 9, respectively. (c) Coordination modes of lactate [(i)–(vi)] and acetate [(vii)–(xi)]. C in black, O in red, Ca in blue, and Ca²⁺ oxide polyhedra in blue. H atoms have been omitted for clarity.

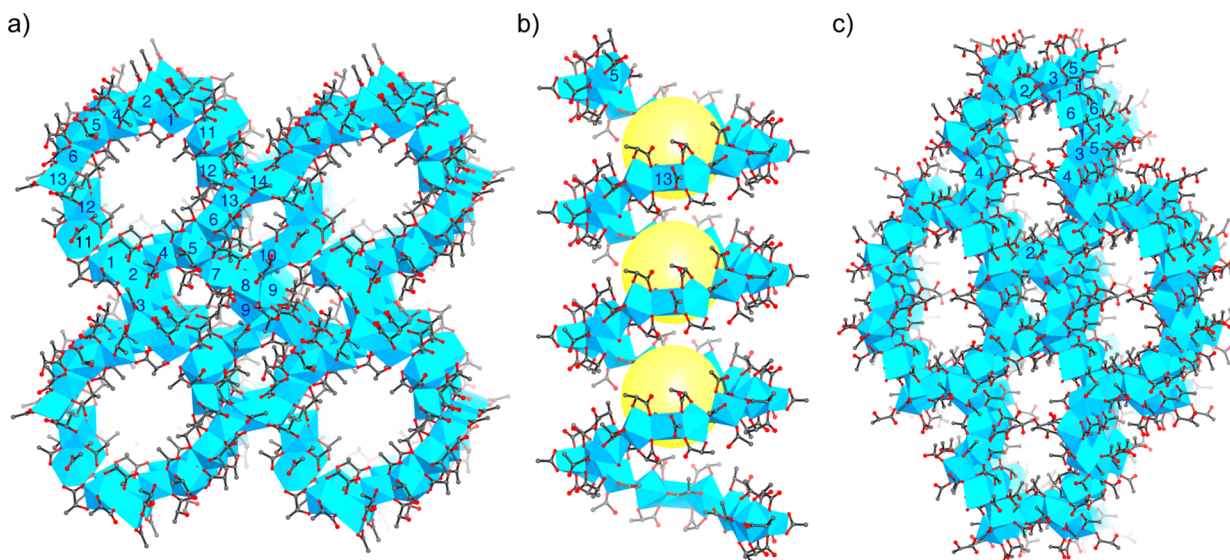


Figure 2. SCXRD structures of (a, b) MOF-1201 and (c) MOF-1203: (a) structure of MOF-1201 viewed along the *b* axis; (b) single helical channel of MOF-1201 viewed along the *a* axis; (c) structure of MOF-1203 viewed along the *a* axis. Channels and pores are illustrated by yellow balls in (b). C in black, O in red, Ca in blue, and Ca²⁺ oxide polyhedra in blue. H atoms have been omitted for clarity.

MOF-1201 has one-dimensional (1D) infinite channels along the *b* axis (Figure 2a). The channels are encompassed by a right-handed single-stranded helical chain (Figure 2a,b) with 16 Ca²⁺ atoms per turn [in the sequence Ca(5), Ca(4), Ca(2), Ca(1), Ca(11), Ca(12), Ca(13), Ca(6), Ca(5), Ca(4), Ca(2), Ca(1), Ca(11), Ca(12), Ca(13), Ca(6)]. The aperture is *ca.* 7.8 Å, and the pitch is *ca.* 13.3 Å. Two adjacent turns are further cross-linked by additional calcium oxide polyhedra. Specifically, two Ca(2) and two Ca(13) centers in each turn are bridged by three calcium

oxide polyhedra [in the sequences Ca(3)–Ca(2)–Ca(3) and Ca(14)–Ca(13)–Ca(14)]. The two Ca(5) and two Ca(11) in each turn are bridged by seven calcium oxide polyhedra [in the sequences Ca(7)–Ca(8)–Ca(9)–Ca(8)–Ca(9)–Ca(8)–Ca(7) and Ca(10)–Ca(8)–Ca(9)–Ca(8)–Ca(9)–Ca(8)–Ca(10); Figure 2a]. The curved bridges result in slightly larger internal pores (*ca.* 9.6 Å) compared with the apertures (*ca.* 7.8 Å).

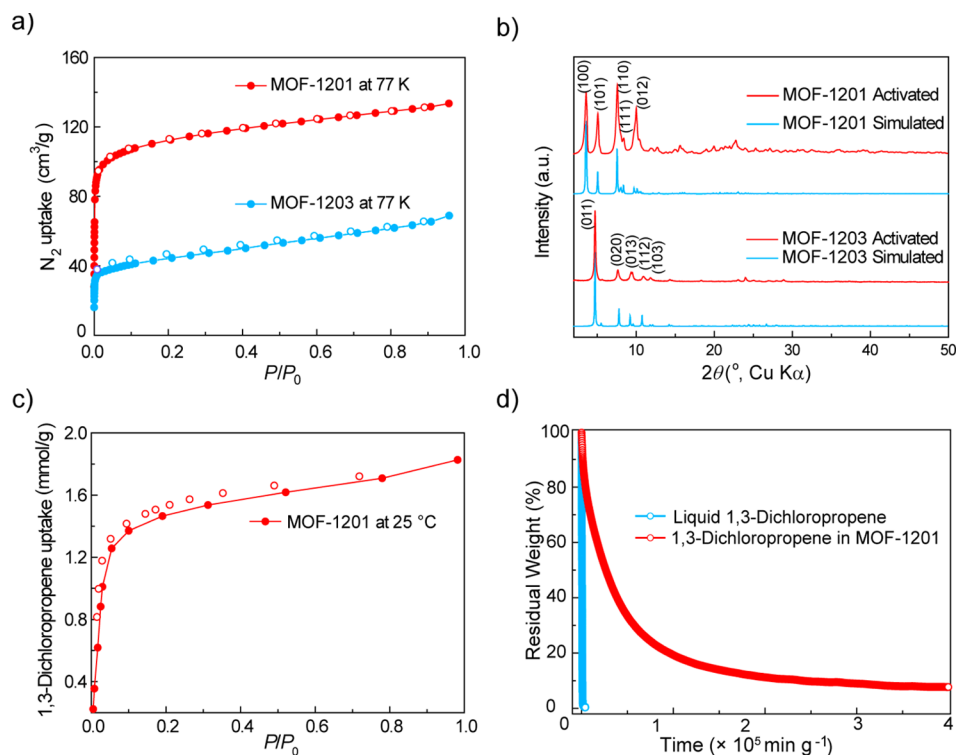


Figure 3. (a) Nitrogen sorption isotherms of MOF-1201 (red) and MOF-1203 (blue) at 77 K (●, adsorption; ○, desorption). (b) PXRD patterns of activated (solvent-free) MOF-1201 and MOF-1203 samples compared with the simulated patterns from the single-crystal structures. (c) *cis*-1,3-Dichloropropene vapor sorption isotherm of MOF-1201 at 25 °C (●, adsorption; ○, desorption). (d) Slow-release traces of pure liquid (blue) and MOF-1201-encapsulated (red) *cis*-1,3-dichloropropene at 25 °C.

MOF-1203 crystallizes in the orthorhombic space group $I2_12_12_1$ and has lattice constants $a = 10.50 \text{ \AA}$, $b = 22.26 \text{ \AA}$, and $c = 31.25 \text{ \AA}$. Six distinct Ca²⁺ centers exist in the structure and are linked by lactate and acetate to form linked calcium oxide polyhedra (Figure 1b). Three coordination modes are found in lactate [(i), (iv), and (v)] and in acetate [(viii), (x), and (xi)] (Figure 1c), with all of the linkers acting as bridges connecting two to four Ca²⁺ centers. For example, Ca(1), Ca(2), and Ca(3) are bridged by an acetate with coordination mode (xi), with Ca(1) coordinated to only one of the carboxylic O, Ca(3) to the other, and Ca(2) to both carboxylic O (Figure S2). Similarly, Ca(3), Ca(4), and Ca(5) are bridged by the same mode and Ca(6), Ca(1), and Ca(5) by mode (i). The resultant framework reveals another type of 1D open channel (Figure 2c), which is surrounded by four calcium oxide polyhedra-based rings [10-membered ring (10 MR)—Ca(6), Ca(1), Ca(5), Ca(3), Ca(1), Ca(6), Ca(1), Ca(3), Ca(5), and Ca(1)] cross-linked by two Ca(4) and two Ca(2) (Figure 2c). The channel has an aperture constructed from 22 calcium oxide polyhedra, but the internal diameter of the channel is smaller than that in MOF-1201 as a result of its rectangular shape; the two incurvate Ca(4) and their linkers further divide the channel into two smaller parts with an aperture of *ca.* 4.6 Å and pore diameter of *ca.* 5.6 Å.

Samples of MOF-1201 and MOF-1203 were solvent-exchanged with ethanol (MOF-1201) and methanol (MOF-1203) for 3 days, followed by direct evacuation under dynamic vacuum (0.04 mbar) at room temperature for 12 h to give solvent-free samples for evaluation of their permanent porosity. Nitrogen sorption measurements at 77 K were then carried out. Both of the frameworks exhibited fully reversible type I isotherms with steep N₂ uptake in the low-pressure region ($P/P_0 < 0.05$) (Figure 3a), indicating the permanent microporosity of these

materials.⁸ The Brunauer–Emmett–Teller (BET) surface areas⁹ of MOF-1201 and MOF-1203 were estimated to be 430 and 160 m² g⁻¹, respectively, from the N₂ isotherms. They have pore volumes of 0.18 and 0.06 cm³ g⁻¹, respectively, which are consistent with those calculated from the single-crystal structures using PLATON.¹⁰ The crystallinity of the solvent-free samples was then checked with powder X-ray diffraction (PXRD). The obtained powder patterns are in good agreement with those simulated from the single-crystal structures, confirming the maintenance of their structural integrity upon activation and the phase purity of the bulk materials (Figures 3b, S3, and S4).

The porosity of MOF-1201 along with its environmentally friendly composition (Ca²⁺, lactate, and acetate) allowed us to explore the potential application of these MOFs in the agriculture industry, where nontoxicity and human and environmental benignity are the most important requirements for a material to be used.^{4,5} Here we demonstrated the use of MOF-1201 as a solid formulation for volatile liquid fumigants.

Fumigants are an important family of pesticides that are widely used to protect plants, especially those of high value (*e.g.*, strawberries and tomatoes), from soil-borne diseases to improve the quality and yield.¹¹ Two volatile liquid compounds, 1,3-dichloropropene (*cis/trans* mixtures) and chloropicrin, have been the most widely used fumigants in large quantities (5.99×10^6 and 4.08×10^6 kg, respectively, in California in 2014).^{11–13}

Commercial formulations of 1,3-dichloropropene and chloropicrin rely on the liquid forms (Telone) applied by shank injection or drip irrigation.¹⁴ However, direct use of the liquids requires high dosages, causing substantial air and groundwater pollution, due to the high volatility and mobility of the liquid chemicals, as well as significant safety hazards to workers during handling and transporting.^{11,14,15}

Sorption-based formulations using porous solids to adsorb fumigants and then slowly release them have emerged as an alternative to suppress the volatility of the chemicals and reduce pollution.¹⁶ Porous matrices such as activated carbon, activated clay, adsorption resin, and activated alumina have been proposed and shown prolonged effective lifetimes of fumigants.¹⁶ However, none of these carrier materials are naturally degradable, which greatly increases their environmental impact as a result of accumulation after implementation.

Sorption of the fumigant *cis*-1,3-dichloropropene by MOF-1201 was carried out here. The adsorption isotherm was measured at 25 °C (Figure 3c) and displays a sharp uptake of 1.4 mmol g⁻¹ (13 wt %) in the low partial pressure range ($P/P_0 = 0.1$), attributed to adsorption within the pores. This uptake was in the range of the values achieved in other porous materials (5–40 wt %) reported in patents.^{16d} Preliminary slow release performance was demonstrated by purging samples of *cis*-1,3-dichloropropene-loaded MOF-1201 and liquid *cis*-1,3-dichloropropene in an air flow of 1.0 cm³ min⁻¹. The sample weight was monitored by a thermogravimetric instrument. As shown in Figure 3d, liquid *cis*-1,3-dichloropropene was released quickly, with 80% of the total weight evaporated within 1000 min g⁻¹. In contrast, the *cis*-1,3-dichloropropene encapsulated in MOF-1201 was released in a much slower manner, with 80% of the total (10.5 wt %) released in 100 000 min g⁻¹, corresponding to 100 times slower release compared with liquid *cis*-1,3-dichloropropene under the same conditions.

The degradability of MOF-1201 was then tested. MOF-1201 can be disassembled in water to give its components, Ca²⁺ ions, lactate, and acetate (Figure S7). It was found that 1 L of water can dissolve 120 ± 10 g of MOF-1201 and that the saturated solution has a nearly neutral pH value (7.6). This property points to MOF-1201 as having the potential to overcome the accumulation issues, thus minimizing adverse effects to the environment but leaving calcium as a nutrient in the soil.¹⁷

To conclude, we have demonstrated the synthesis of the first examples of eco-friendly porous Ca²⁺ MOFs constructed from nontoxic, renewable lactate linkers. The use of MOF-1201 as a degradable carrier for pesticides represents an important step toward using such MOFs in applications dealing with the agriculture and food industries.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b04542.

Synthesis and additional data (PDF)

Crystallographic data for MOF-1201 (CIF)

Crystallographic data for MOF-1203 (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) Yaghi, O. M.; O'Keeffe, M.; Ockwig, N. W.; Chae, H. K.; Eddaoudi, M.; Kim, J. *Nature* **2003**, *423*, 705–714. (b) Kaskel, S. *The Chemistry of Metal–Organic Frameworks: Synthesis, Characterization, and Applications*; Wiley-VCH: Weinheim, Germany, 2016.
- (2) Furukawa, H.; Cordova, K. E.; O'Keeffe, M.; Yaghi, O. M. *Science* **2013**, *341*, 1230444.
- (3) (a) Schröder, M. *Functional Metal–Organic Frameworks: Gas Storage, Separation and Catalysis*; Springer: Berlin, 2010. (b) Li, J.-R.; Sculley, J.; Zhou, H.-C. *Chem. Rev.* **2012**, *112*, 869–932.
- (4) Forgan, R. S. *Metal–Organic Frameworks: Edible Frameworks*. In *Encyclopedia of Inorganic and Bioinorganic Chemistry*; John Wiley & Sons: New York, 2014.
- (5) Imaz, I.; Rubio-Martínez, M.; An, J.; Solé-Font, I.; Rosi, N. L.; Maspocho, D. *Chem. Commun.* **2011**, *47*, 7287–7302.
- (6) Fromm, K. M. *Coord. Chem. Rev.* **2008**, *252*, 856–885.
- (7) National Library of Medicine. TOXNET. <https://toxnet.nlm.nih.gov/index.html> (accessed May 3, 2017). Calcium lactate and acetate are generally recognized as safe (GRAS) food additives.
- (8) Thommes, M.; Kaneko, K.; Neimark, A. V.; Olivier, J.; Rodriguez-Reinoso, F.; Rouquerol, J.; Sing, K. S. *Pure Appl. Chem.* **2015**, *87*, 1051–1069.
- (9) Walton, K. S.; Snurr, R. Q. *J. Am. Chem. Soc.* **2007**, *129*, 8552–8556.
- (10) Spek, A. L. *Acta Crystallogr.* **2009**, *D65*, 148–155.
- (11) (a) Shorter, J. H.; Kolb, C. E.; Crill, P. M.; Kerwin, R. A.; Talbot, R. W.; Hines, M. E.; Harriss, R. C. *Nature* **1995**, *377*, 717–719. (b) Martin, F. N. *Annu. Rev. Phytopathol.* **2003**, *41*, 325–350.
- (12) Ashworth, D. J.; Yates, S. R.; Van Wessenbeeck, I. J.; Stanghellini, M. *J. Agric. Food Chem.* **2015**, *63*, 415–421.
- (13) California Department of Pesticide Regulation. Pesticide Use Reporting—2014 Summary Data. http://www.cdpr.ca.gov/docs/pur/pur14rep/14_pur.htm (accessed May 3, 2017).
- (14) Kim, J.-H.; Papiernik, S. K.; Farmer, W. J.; Gan, J.; Yates, S. R. *J. Environ. Qual.* **2003**, *32*, 2223–2229.
- (15) (a) Yates, S. R.; Ashworth, D. J.; Zheng, W.; Zhang, Q.; Knuteson, J.; van Wessenbeeck, I. J. *J. Agric. Food Chem.* **2015**, *63*, 5354–5363. (b) Desaeger, J. A.; Eger, J. E. J.; Csinos, A. S.; Gilreath, J. P.; Olson, S. M.; Webster, T. M. *Pest Manage. Sci.* **2004**, *60*, 1220–1230.
- (16) (a) Akira, S.; Mizuyoshi, F.; Hiroshi, A.; Shiyunosuke, W.; Nobuji, T. Granular chloropicrin preparation for soil disinfection and production thereof. Japan Patent JPH01172302(A), July 7, 1989. (b) Solar, J. M.; Wilson, C. L.; Ghaouth, A. E. Controlled release fumigation of harvested agricultural commodities. U.S. Patent US5958490A, Sept 28, 1999. (c) Han, J. L. Mixed solid preparation of chloropicrin and 1,3-dichloropropylene and manufacturing technology thereof. China Patent CN101627754B, Nov 13, 2013. (d) Han, J. L.; Yi, C. J. Preparation method and application of 1,3-dichloropropene solid slow-release preparation. China Pat. Appl. CN201310062631, May 22, 2013.
- (17) Engelstad, O. P. *Fertilizer Technology and Use*; Soil Science Society of America: Madison, WI, 1985.