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Controlled release of H₂S and NO gases through CO₂-stimulated anion exchange

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Difficulties related to handling gases are a common bottleneck for applications. Although solid materials that release gas molecules under external stimuli exist, they require an external energy or a device for reliable operation. Herein, we report a CO₂ stimulus for controlled release of p.p.m.-level functional gases from solid materials. A CO₂-preferential anion-exchange property of layered double hydroxides and redox reactions in gas molecules are combined to release various gases (including H₂S and NO) under ambient air from HS⁻ and NO₂⁻-incorporated layered double hydroxides, respectively. The profiles of gas release are mainly governed by the difference of pK_a between H₂CO₃ and resulting acids (formed through protonation of interlayer anions), and are not so susceptible to the variation of relative humidity in air. Moreover, structural modulation of solid materials enables fine control of the gas release profiles. The use of safe, ubiquitous, and nearly constant (~400 p.p.m. in atmosphere) CO₂ stimulus offers broad applications for functional gases.

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Gas molecules play key roles in many research fields and their practical utility depends on the safety and cost-effectiveness of the gas delivery system (particularly when gases are toxic, labile, or flammable)^{1–3}. The use of high-pressure gas cylinders is often the source of safety concerns; therefore, solid materials that release gas molecules under external stimuli (e.g., heat, light, and vacuum) have attracted particular interest^{4–6}. However, such conventional stimuli require external energy (e.g., electricity) and controlling device for reliable operation. By contrast, the use of aerial components as stimuli for gas release is attractive in that air is safe, charge-free, and available anytime anywhere. Some zeolites and metal organic frameworks that capture and release gases have been reported^{7–9}. In particular, controlled release of H₂S and NO is valuable for medical application, because these gases are physiologically active (i.e., they exhibit effects such as anti-inflammatory, anti-oxidative, cytoprotective, and vasodilatory effects) at p.p.m.-level concentrations but are toxic at higher concentrations and labile under air^{10–12}. These solids bind gases at coordinatively unsaturated transition metal cation sites and release them under moist air through the replacement of gas molecules with water. However, the water-triggered gas-release system could be susceptible to the variation of relative humidity (RH) and long-term release of gases were, in most cases, demonstrated under fixed and low RH condition (10–20%RH)^{7,8}. In addition, initial burst release of highly concentrated gases tends to be observed.

Layered double hydroxides (LDHs) are inorganic layered materials with the general formula $M^{II}_yM^{III}_x(OH)_{2(y+x)}(X^{n-})_m \cdot nH_2O$, where M^{II} , M^{III} , X^{n-} , and mH_2O are, respectively, a divalent metal cation (y is in the range of 2–4), a trivalent metal cation, an n -valent anion, and hydrated water (m depends on the humidity of the environment) (Fig. 1)¹³. $M^{II}_yM^{III}_x(OH)_{2(y+x)}$ forms a positively charged two-dimensional (2D) layer and both charge-compensating anion (X^{n-}) and hydrated water (mH_2O) are located within the interlayer. Previously, we reported that some conjugate anions of weak acids (e.g., acetate and carbonate) in the interlayer of Mg/Al-type LDHs tend to get exchanged with CO_3^{2-} derived from aerial CO_2 ^{14–16}. The CO_2 -stimulated anion-exchange phenomenon at the air–solid interface inspired us to explore a novel class of gas-releasing materials.

Herein, we report solid materials that autonomously release functional gases in response to CO_2 stimulus. Anions of weak acids (Z^- ; $pK_a > 2$) involved in the interlayer of Mg/Al-type LDHs can be protonated by H_2CO_3 ($pK_a = 3.6$) derived from aerial CO_2 and interlayer H_2O , leading to autonomous release of protic gases (HZ) (Fig. 1b, eq. 1). Interlayer HS^- or NO_2^- in LDHs is protonated with aerial CO_2 and H_2O , resulting in the autonomous release of H_2S or HNO_2 under air (Fig. 1b, eq. 2 and 3). HNO_2 is convertible to NO through an automatic disproportionation reaction or subsequent treatment with a reducing agent (Fig. 1b, eq. 4 and 5)¹⁷. Although there are some precedent reports of generating NO from NO_2^- through chemical reaction in solution^{18–22}, NO_2^- -incorporated LDHs offer all-solid system for NO release. Profiles (concentration and duration) of gas release are basically dependent on the pK_a of the resulting acids, because the protonation equilibrium between interlayer anions and H_2CO_3 (from CO_2 and H_2O) governs the chemical events. We also demonstrate that profiles of gas release can be controlled by various factors such as chemical composition of LDHs, diffusion of gases and ions, and chemical equilibrium. The profiles of gas release from LDH are not so susceptible to the variation of RH due to abundant water inherently present in the interlayer. This could be advantageous for release of functional gases under ambient air, because RH is quite variable from moment to moment. In contrast, concentration of CO_2 in ambient air is almost constant (around ~400 p.p.m.), offering controlled release

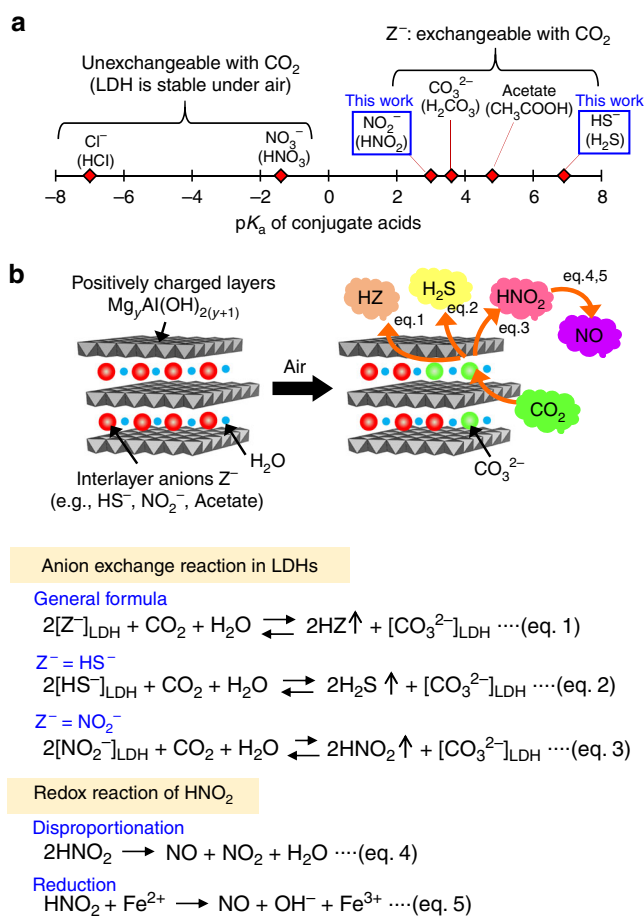


Fig. 1 Design of solid materials that release functional gases in response to CO_2 . **a** Susceptibility of interlayer anions (Cl^- , NO_3^- , NO_2^- , CO_3^{2-} , acetate, and HS^-) of LDHs for CO_2 -stimulated anion exchange, showing correlation with pK_a values of the conjugate acids. Z^- denotes a conjugate base of volatile weak acid. **b** Release of various gases (HZ, H_2S , HNO_2 , or NO) from LDHs through anion exchange between interlayer anions (Z^- , HS^- , or NO_2^-) and aerial CO_2 (eq. 1–3), disproportionation (eq. 4), and reduction (eq. 5). Note that interlayer- and aerial- H_2O are available in eq. 1–3.

of functional gases without precise adjustment of conditions for gas release. Moreover, Mg/Al-type LDHs is transition-metal-free and biocompatible²³. Thus, our low-cost and safe-to-handle materials are feasible for creating a disposable medical system for a controlled release of p.p.m.-level physiologically active gases under ambient air.

This work reveals that LDH is an attractive material for gas release and the CO_2 -driven system is potentially useful for expanding opportunities of utilizing functional gases in society.

Results and discussion

Synthesis and characterization of H_2S -releasing LDHs. LDHs involving HS^- or S^{2-} , for H_2S release, were synthesized by two-step anion-exchange reactions²⁴. As starting materials, CO_3^{2-} -type LDHs with Mg:Al ratio of 3:1 ($Mg_3Al(OH)_8(CO_3^{2-})_{0.5} \cdot 2H_2O$) and 2:1 ($Mg_2Al(OH)_6(CO_3^{2-})_{0.5} \cdot 2H_2O$) were utilized. The former is commercially available and the latter was synthesized by a hydrothermal reaction²⁵. As CO_3^{2-} of LDH is hardly exchangeable with other anions under normal anion-exchange conditions, CO_3^{2-} in LDH was first replaced with Cl^- using reported de-intercalation method²⁶. Then, the resulting Cl^- -type LDHs (Mg:Al = 2:1 or 3:1) dispersed in degassed deionized water were reacted with 10 equivalent (in mole) of $NaHS \cdot nH_2O$ or

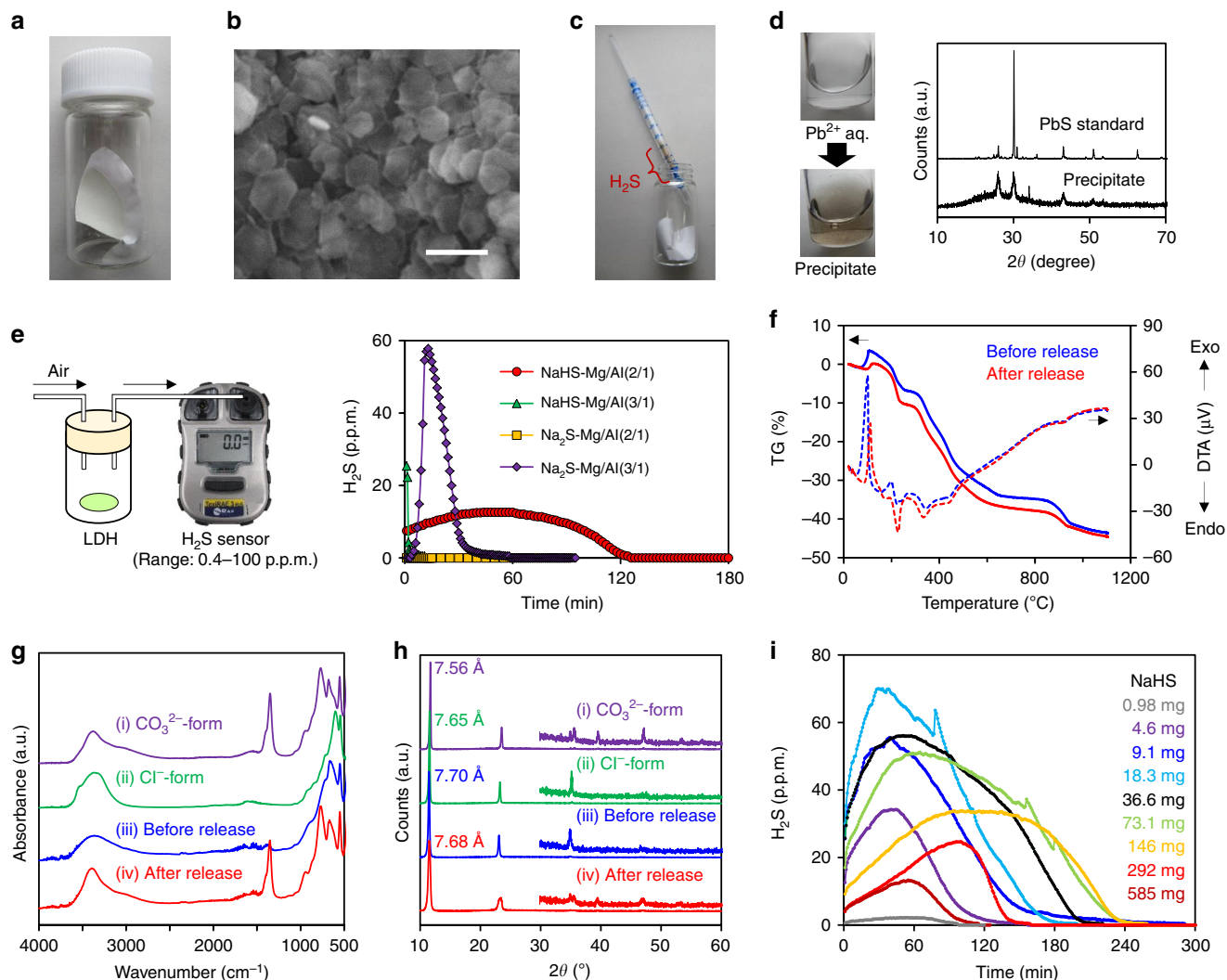


Fig. 2 Characterization of H₂S-releasing layered double hydroxides. **a** Photograph of NaHS-Mg/Al(2/1) embedded on membrane filter (stored in the glass vial purged with dry N₂). **b** SEM image of NaHS-Mg/Al(2/1) after H₂S release (scale bar: 2 μm). **c** H₂S release from NaHS-Mg/Al(2/1) confirmed by detector tube. **d** Powder XRD pattern of black precipitate obtained by reaction of aqueous Pb²⁺ with released gas. **e** Continuous monitoring of H₂S released from LDHs under standard flow condition; 0.020 mmol of LDHs (5.0 mg of Mg/Al(2/1) and 6.25 mg of Mg/Al(3/1)) were tested. Thermogravimetry-differential thermal analysis (TG-DTA) profiles (**f**), IR spectra (**g**), and powder XRD patterns (**h**) of NaHS-Mg/Al(2/1) before and after H₂S release. For comparison, IR and XRD data of starting materials are also shown. **i** Optimizing amount of NaHS·*n*H₂O used in preparing NaHS-Mg/Al(2/1) from 40 mg of Cl⁻-type LDH; 20 mg of LDH was tested under standard flow condition.

Na₂S·9H₂O for 2 days under N₂, as summarized in Supplementary Table 1. Solid materials were collected by filtration, washed with degassed deionized water, and then dried in vacuum (all performed under N₂ atmosphere) to afford four types of products (NaHS-Mg/Al(2/1), NaHS-Mg/Al(3/1), Na₂S-Mg/Al(2/1), and Na₂S-Mg/Al(3/1)); see Fig. 2a for a typical image). The products were preserved in a sealed pack for isolation from air (Supplementary Fig. 9). As far as we know, HS⁻ or S²⁻-incorporated LDHs produced in an inert atmosphere throughout syntheses and preservation have not been reported. Although there are some reports that claim the synthesis of HS⁻ or S²⁻-incorporated LDHs, they were synthesized and/or preserved under air^{27,28}. As these materials are sensitive to air, their products produced without care about atmosphere must be different from ours. A scanning electron microscopy (SEM) image showed that the morphology (hexagonal plate) of LDH was maintained after multi-step anion-exchange reactions (Fig. 2b).

NaHS-Mg/Al(2/1) released odor characteristic to H₂S for over 1 h when exposed to air [CAUTION!!] and the response of the

detector tube was positive (Fig. 2c). In addition, the released gas was confirmed as H₂S through the formation of PbS upon interaction with Pb²⁺ (Fig. 2d). Moreover, SO₂ was not detected (<0.01 p.p.m.) in ~10 p.p.m. H₂S by the detector tube. The concentration of H₂S released from LDHs was continuously monitored by an electrochemical sensor under the standard flow conditions employed in this study (air, 50%RH, 100 mL min⁻¹, 20 °C) and NaHS-Mg/Al(2/1) demonstrated a release of ~10 p.p.m. H₂S for 2 h (Fig. 2e). On the other hand, Na₂S-Mg/Al(2/1) did not release H₂S. NaHS-Mg/Al(3/1) and Na₂S-Mg/Al(3/1) released concentrated (over 25 p.p.m.) H₂S, but the release duration was not as long as that of NaHS-Mg/Al(2/1). A release profile of NaHS-Mg/Al(2/1) can be explained by a narrow interlayer distance of Mg/Al = 2/1-type LDHs¹⁶, which suppresses the interaction between interlayer anions and aerial components.

Thermogravimetry-differential thermal analysis showed that NaHS-Mg/Al(2/1) involves HS⁻, which demonstrate exothermal oxidation into S₂O₃²⁻ at around 65–100 °C in air (Fig. 2f)^{27,28}. In contrast, exothermal signals were not observed for Na₂S-Mg/Al

(2/1) at 65–100 °C, indicating that sulfur sources were not incorporated (Supplementary Fig. 10). After H₂S release ceased, Fourier-transform infrared (IR) and powder X-ray diffraction (XRD) analyses of NaHS-Mg/Al(2/1) indicated that HS⁻ was partly replaced with CO₃²⁻ (Fig. 2g, h), supporting the CO₂-stimulated anion-exchange mechanism. After H₂S release, only a trace amount of S₂O₃²⁻ (1000–1200 cm⁻¹) was observed in the IR spectrum of NaHS-Mg/Al(2/1). In contrast, NaHS-Mg/Al(3/1), which ceased H₂S release within a few minutes (Fig. 2e), showed an intense IR signal from S₂O₃²⁻ due to HS⁻ oxidation (Supplementary Fig. 11)²⁸. Thus, HS⁻ tolerance against aerial oxidation is a crucial factor for long-term release of H₂S.

The amount of NaHS·*n*H₂O used in the synthesis of NaHS-Mg/Al(2/1)-type LDH was varied to find the optimum condition for obtaining the largest H₂S release (Fig. 2i). The concentration of the released H₂S increased with an increase in the amount of NaHS·*n*H₂O from 0.98 mg to 18.3 mg for 40 mg Cl⁻-type LDH and the gross release reached maximum at 36.6 mg NaHS·*n*H₂O (=2.6 equivalent in mole for Cl⁻). However, further addition of NaHS·*n*H₂O would reduce the gross release of H₂S, presumably due to increased basicity (i.e., OH⁻) and impurities involved in the reaction solution.

Assuming that the chemical composition of NaHS-Mg/Al(2/1) with a maximum gross release is Mg₂Al(OH)₆(HS⁻)·2H₂O (Mw = 246.8 g mol⁻¹), 20 mg of the product involves 81 μmol of HS⁻, which corresponds to a release of 76 p.p.m. H₂S for 240 min (under 100 mL min⁻¹). The actual amount of H₂S released from NaHS-Mg/Al(2/1) was about half the expected value (Fig. 2i), which is attributable to an incomplete anion exchange from Cl⁻ to HS⁻ (see Supplementary Discussion and Supplementary Fig. 21 for discussion on chemical formula of NaHS-Mg/Al(2/1)).

It is widely known that NaHS and Na₂S also release odor characteristic to H₂S and we confirmed that these simple salts release H₂S under air (Supplementary Fig. 12). H₂S has rather high pK_a so that even simple salts can participate in CO₂-stimulated protonation equilibrium. However, these salts are deliquescent and strongly basic (pH ≥ 12). In contrast, NaHS-Mg/Al(2/1) is non-deliquescent, insoluble in water, and nearly neutral (pH ≈ 8), even when wet with water (Supplementary Fig. 12). Moreover, LDHs offer fine control of H₂S release by tuning of their chemical compositions. Mg/Al-type LDH, known as hydrotalcite, is toxic-heavy-metal-free, biocompatible, and practically utilized as an antacid drug²³. These features of LDHs are advantageous for medical applications.

We note a fundamental importance of LDH in gas release. Our previous study¹⁵ revealed that interlayer CO₃²⁻ of LDH is dynamically exchanging with aerial CO₂, although CO₃²⁻ of a simple salt (¹³C-labeled Na₂CO₃) did not exchange. The result implies that interlayer anions in LDH is activated to CO₂-stimulus due to 2D structure and high affinity of LDH to CO₂ (while contact of interlayer anions and aerial components is appropriately regulated). The concept is generally applicable and will guide a design of controlled release of various types of gases.

Controlled release of H₂S from LDHs. To reduce the interaction between NaHS-Mg/Al(2/1) and air for longer H₂S release, assembled materials with LDHs wrapped with porous tapes were prepared. About 1.1 mg of NaHS-Mg/Al(2/1), which was synthesized under the optimum conditions using 40 mg LDH and 36.6 mg NaHS·*n*H₂O (Fig. 2i), was sandwiched between the membrane filters and further between the porous tapes (Fig. 3a and see Supplementary Fig. 13 for details). As a result, the H₂S release profile was significantly improved compared to that of the bare (i.e., noncovered) material (Fig. 3b). In addition, this patch-like assembly was effective in holding the LDH powder.

The H₂S release profiles of the patch-like assembly were investigated under various conditions to probe the mechanisms and controllability of H₂S release. The H₂S concentration was almost proportional to the number of patches (Fig. 3b), which indicates ease of control of the gas concentration. The flow rate also affects the measured concentration: the H₂S concentration was inversely proportional to the flow rate of air (Fig. 3c). This means that the quantity of H₂S released from LDHs was almost constant. The RH in air did not affect so much on the concentration of H₂S (under practical range; 10~87%RH), although the concentration reduced for several times under fully dry air (Fig. 3d). H₂S release was not observed under dry N₂ and O₂ (Fig. 3e), but addition of humidity to N₂ induced H₂S release (Fig. 3f) due to the presence of equilibrium between interlayer HS⁻ and H₂O (i.e., [HS⁻]_{LDH} + H₂O → H₂S↑ + [OH⁻]_{LDH}). Addition of CO₂ into dry N₂ also caused H₂S release (Fig. 3g) and it is clear that the gas release from LDHs is strongly dependent on CO₂ concentration. However, CO₂ concentration in air is almost constant (~400 p.p.m.), which is in contrast to RH that can change dramatically from moment to moment. In this process, the proton source must be interlayer H₂O and the overall reaction is expressed as 2[HS⁻]_{LDH} + CO₂ + [H₂O]_{LDH} → 2H₂S↑ + [CO₃²⁻]_{LDH}. The activity of H₂S release was gradually quenched when exposed to dry O₂ beforehand, which is attributable to HS⁻ oxidation (Supplementary Fig. 14). The H₂S concentration was slightly increased when heated to 36 °C (Fig. 3h), presumably due to accelerated diffusion of gas molecules and anions within the interlayer. LDHs preserved in a sealed pack for six months demonstrated a rather flat and elongated H₂S release (Fig. 3i). Mechanism of the aging effect could be homogenized distribution of HS⁻ within the interlayer. In fact, the aging effect can be accelerated by thermal treatment (e.g., 60 °C for several days) (see Supplementary Discussion and Supplementary Fig. 15 and 23 for discussion on the aging effect).

Controlled release of NO from LDHs. LDHs involving NO₂⁻ were synthesized from Cl⁻-type LDHs (Mg:Al = 2:1 or 3:1) and NaNO₂, yielding NaNO₂-Mg/Al(2/1) and NaNO₂-Mg/Al(3/1) (183 mg NaNO₂ used for 40 mg LDHs; see Supplementary Method, Discussion, and Fig. 22 for optimization of mixing ratio and discussion on chemical formula of the product). Release of HNO₂ from NaNO₂-Mg/Al(3/1) under air is suggested by visible color change of Griess reagent, which is a NO₂⁻ indicator²⁹ (Fig. 4a). The detector tube for NO + NO₂ demonstrates a positive response (0.7 p.p.m.) for gases released from 100 mg NaNO₂-Mg/Al(3/1) under air (Fig. 4b). It is noteworthy that the detector tube for NO + NO₂ (“Tube-A”) was equipped with the strong oxidant (Cr⁶⁺ + H₂SO₄) part at the entry for conversion of NO to NO₂ and its response should also involve the contribution of HNO₂. Thus, the total concentration, NO + NO₂ + HNO₂, was 0.7 p.p.m. The concentration of nitrogenous gases released from LDHs was two to three orders of magnitude lower than that of H₂S, because H₂CO₃ formed by CO₂ and water can afford fewer protons to NO₂⁻ than that to HS⁻ due to lower pK_a of HNO₂ (= ~3.0)³⁰. On the other hand, release of nitrogenous gases was much longer, and continued for at least one day, maintaining similar concentration. Besides, NO₂ measured by another type of detector tube without the oxidant part (“Tube-B”) was 0.2 p.p.m. NO was measured by combining two detector tubes, as follows. First, NO₂ and HNO₂ were removed by detector tube “B” for NO₂, which contains *o*-tolidine (aromatic amine) as an indicator. Here, acidic HNO₂ was removed by passing through this tube, but did not change color of the tube. In fact, after this treatment, the released gas did not change color of the Griess reagent, indicating complete removal of HNO₂ together with NO₂. Then, NO was determined

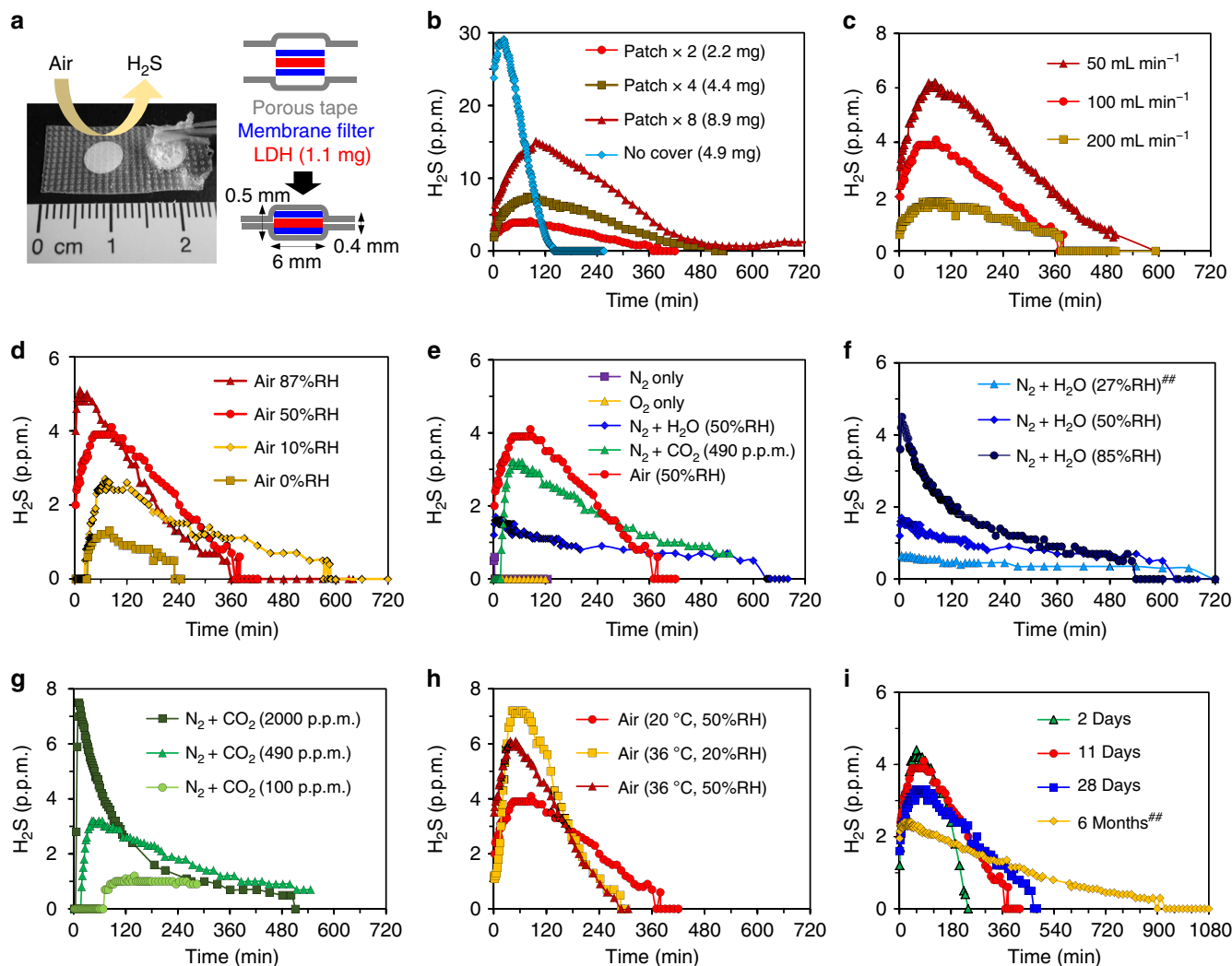


Fig. 3 H₂S release profiles from NaHS-Mg/Al(2/1) sandwiched between porous tapes. **a** Photograph and illustration of H₂S release patches. One patch contains 1.1 mg of LDH. **b–i** Influences of various factor for H₂S release profiles[#]; **b** patch numbers (release from noncovered sample is also shown for comparison), **c** flow rate of air, **d** humidity in air, **e** type of carrier gases, **f** humidity in N₂, **g** CO₂ concentration in dry N₂, **h** effect of temperature and humidity, and **i** aging effect. [#]Unless noted, H₂S release from two patches was tested under the standard flow condition. ^{##}Release from four patches was halved. See Supplementary Figs. 1 and 2 for experimental set-up.

as 0.2 p.p.m. by the next detector tube, “A” for NO + NO₂. Thus, HNO₂ was estimated to be 0.3 p.p.m. by subtracting 0.2 p.p.m. of NO₂ and 0.2 p.p.m. of NO from the total 0.7 p.p.m. The release of equal amounts (0.2 p.p.m.) of NO and NO₂ indicates that these gases are derived from the disproportionation of HNO₂ (eq. 4 in Fig. 1b). Release of nitrogenous gases (NO + NO₂ + HNO₂) under air flow (100 mL min⁻¹) increased a little with humidity (0.5 p.p.m. at 1.8%RH, 0.7 p.p.m. at 35%RH, 1.1 p.p.m. at 82%RH, and 1.6 p.p.m. at 90%RH), but maintained similar order of concentration under practical RH (i.e., 35–90%RH).

Compared with NaNO₂-Mg/Al(3/1), release of nitrogenous gases from NaNO₂-Mg/Al(2/1) was considerably small in air (~0.1 p.p.m. or less) in the initial 2 h, whereas that of gases was gradually increased to ~1.5 p.p.m. when the sample was further left in air. This delayed release profile resembles the case of NaHS-Mg/Al(2/1), where the anion-exchange reaction was regulated due to the narrow interlayer space.

Exhaled breath (4.0% CO₂, nearly saturated humidity, 100 mL min⁻¹) was applied to 100 mg NaNO₂-Mg/Al(3/1) for promoting protonation of interlayer NO₂⁻ (eq. 3 in Fig. 1b) and NO, NO₂, and HNO₂ measured by detector tubes were 1.0, 1.1, and 5.9 p.p.m.,

respectively (Fig. 4c). HNO₂ can be reduced to NO using Fe²⁺ (eq. 5 in Fig. 1b)¹⁷, and insertion of the FeSO₄·7H₂O column into the flow line successfully increased NO concentration to 6.6 p.p.m. (Fig. 4d). NO₂ was decreased to 0.55 p.p.m., presumably due to partial reduction to NO and/or adsorption on FeSO₄·7H₂O. The total amount of nitrogenous gases (NO + NO₂ + HNO₂) was ~7.0 p.p.m., which means that the unreacted HNO₂ was negligible. The remaining NO₂ could be removed down to 0.02 p.p.m. (only twice of the atmospheric level) using Mg(OH)₂, a selective adsorbent for acidic gases (Fig. 4e)^{31,32}.

Release of NO from NaNO₂-Mg/Al(3/1) under exhaled breath continued over 2 weeks, as monitored by an electrochemical NO sensor, and its half-life of release was ~6 days (Fig. 4f and see Supplementary Fig. 16 for enlarged image). The NO concentration did not increase in proportion to the quantity of materials (block connection in Fig. 4g). On the other hand, when NaNO₂-Mg/Al(3/1) and FeSO₄·7H₂O were alternatively connected (Fig. 4g), the NO concentration could be increased in proportion to the quantity of the materials. This is because HNO₂ generation reached saturation under chemical equilibrium (eq. 3 in Fig. 1b) in case of block connection, whereas HNO₂ was converted to

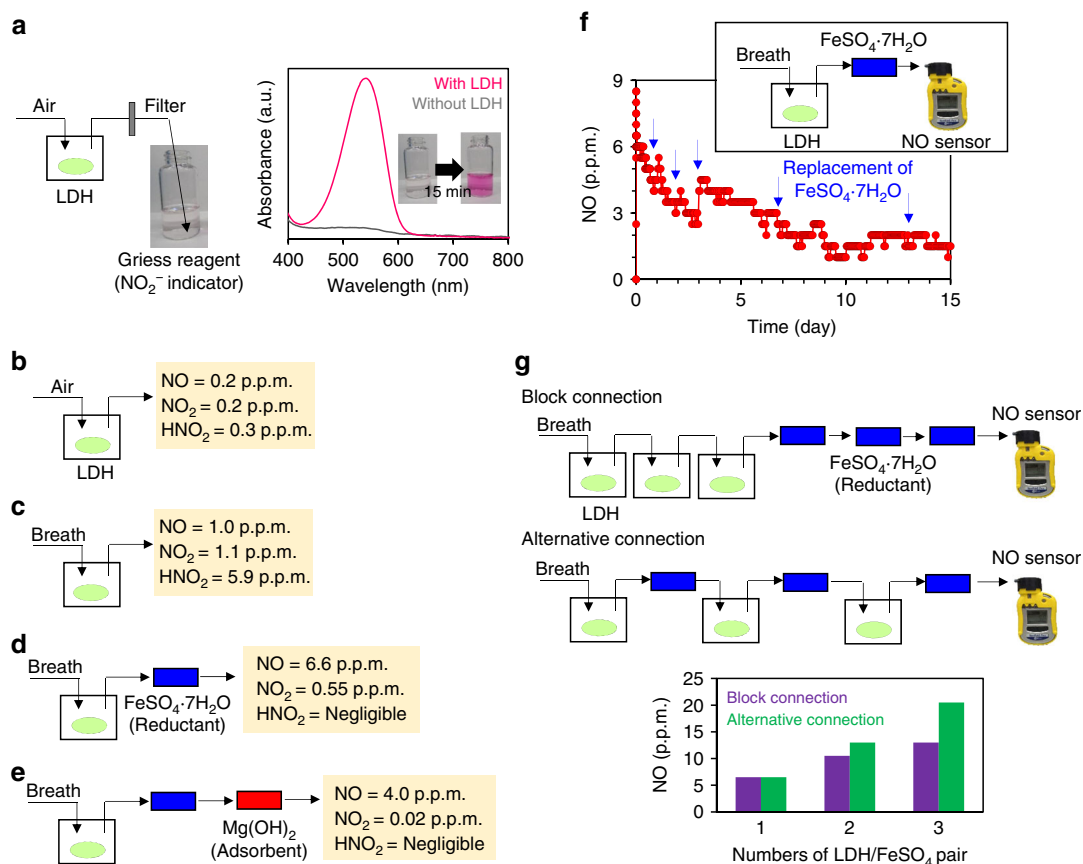


Fig. 4 Release of HNO₂ and conversion to NO. **a** Color change of Griess reagent showing the presence of HNO₂. **b–e** Concentrations of NO, NO₂, and HNO₂ released from 100 mg NaNO₂-Mg/Al(3/1) (determined by detector tube). See Supplementary Fig. 3 for experimental details. Air (20 °C, 35%RH) or exhaled breath were applied at flow rate of 100 mL min⁻¹. Released gases were passed through FeSO₄·7H₂O and Mg(OH)₂ loaded in the glass tube. **f** NO-release profile from 100 mg NaNO₂-Mg/Al(3/1) under exhaled-breath flow (50 mL min⁻¹). FeSO₄·7H₂O was occasionally replaced with new ones (indicated by blue arrow). See Supplementary Fig. 4 for experimental details. **g** Tandemly connected NaNO₂-Mg/Al(3/1) and FeSO₄·7H₂O (in block or alternative manner) for accumulating the concentration of NO under exhaled-breath flow (50 mL min⁻¹). Each vial contains 100 mg NaNO₂-Mg/Al(3/1). The NO concentration is monitored after stabilization for 15 min.

neutral NO in each step without disturbing HNO₂ generation in the next step in case of the alternative connection.

The IR spectra of the as-prepared NaNO₂-Mg/Al(3/1) showed an intense absorption band of NO₂⁻ at 1227 cm⁻¹ (Supplementary Fig. 16). After the LDH was exposed to exhaled breath for 2 weeks, the NO₂⁻ signal was reduced, yet the CO₃²⁻ signal at 1360 cm⁻¹ increased. This result indicates the dominant role of the CO₂-triggered anion-exchange reaction for HNO₂ release. XRD analyses also supported these results (Supplementary Fig. 16).

Battery-free respirator for inhaled NO. The potential utility of the gas release system was demonstrated by creating a portable and battery-free respirator that can supply therapeutically useful quantity of NO into inhaled air. NO becomes a selective and fast-acting pulmonary vasodilator upon inhalation, and inhaled NO is a well-established method for treating respiratory distress such as persistent pulmonary hypertension of the newborn^{33–36}. However, current inhaled NO is an advanced medical treatment since it requires a high-pressure gas cylinder, expensive medical instrument, and trained operator for controlling/monitoring the purity and dose of NO^{35,36}. The typical concentration of NO used for treatment of respiratory distress is 5–20 p.p.m.^{33–36} and the respiratory volume of newborns and infants is ~0.5–2.5 L min⁻¹. Although the NO-release systems described in Fig. 4b–g, which

are based on spatially isolated LDH and a reducing agent, provided NO over two weeks, limited quantity of NO (~1 p.p.m. NO, 100 mL min⁻¹) could be obtained from 100 mg NaNO₂-Mg/Al(3/1) under air. Thus, it will require gram scale of materials to satisfy the criteria (5–20 p.p.m., 0.5–2.5 L min⁻¹) of inhaled NO. In contrast, the results of Fig. 4g suggest that a spontaneous conversion of HNO₂ into NO is effective for NO accumulation (as a result of forwarding eq. 3 in Fig. 1b). Thus, we attempted to mix NaNO₂-Mg/Al(3/1) (100 mg) and FeSO₄·7H₂O (1.0 g) in powder form, and found that injection of wet air (saturated humidity, 100 mL min⁻¹) to the mixture led to release of highly concentrated NO (up to 650 p.p.m.) [CAUTION!!]. It is noted that preparation of wet air (with saturated humidity) is much easier than preparing air with other fixed humidity (e.g., 10%RH). After dilution with ambient air (4.0 L min⁻¹), 5–16 p.p.m. NO was obtained for about 1 h (Fig. 5a). The use of Mg(OH)₂ effectively reduced the concentration of contaminated NO₂ to 0.03–0.075 p.p.m., which is much lower than the permissible limit of concentration determined by the U.S. Environmental Protection Agency (=1 p.p.m.)³⁷. It is noteworthy that mixing of NaNO₂ and FeSO₄·7H₂O caused a burst release of NO [CAUTION!!] due to rapid reaction of NO₂⁻ and Fe²⁺ (Supplementary Fig. 17e).

The RH required to initiate NO release from the mixture was more than 60% (Supplementary Figs. 6 and 17a) and the NO concentration could be adjusted by manipulating the RH (Supplementary Fig. 17b). Moreover, we found that wet N₂ is

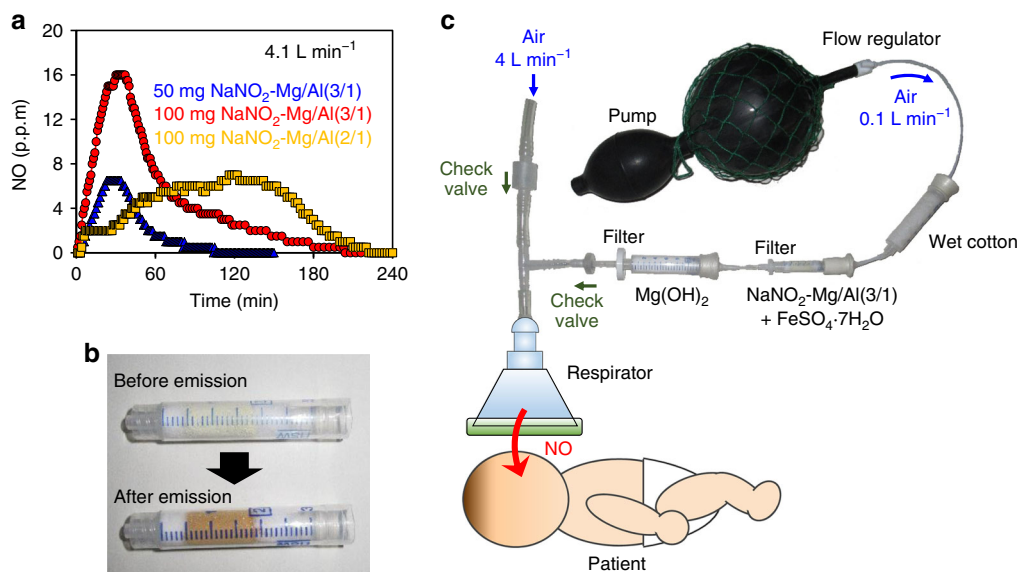


Fig. 5 Battery-free respirator for inhaled NO. **a** Concentration of NO released from the mixture of NO₂⁻-incorporated LDH and 10 equivalent (in weight) of FeSO₄·7H₂O under 4.1 L min⁻¹ air. See Supplementary Fig. 5 for experimental set-up. **b** Photograph of NaNO₂-Mg/Al(3/1) and FeSO₄·7H₂O mixture before and after ending of NO release. **c** Prototype portable and battery-free respirator for inhaled NO.

also applicable (Supplementary Fig. 17c). NO release under wet N₂ indicates that it is not governed by CO₂-triggered anion exchange and a plausible mechanism is that the direct anion exchange between NO₂⁻ and SO₄²⁻ occurred in the mixed solids in a similar way as that reported for the anion exchange of LDHs in KBr powder³⁸ (Supplementary Fig. 18a). Accordingly, self-reactive Fe(NO₂)₂ was formed outside LDHs, and then NO₂⁻ was reduced to NO by Fe²⁺. This hypothesis is supported by powder XRD patterns of post-release mixtures of NaNO₂-Mg/Al(3/1) and FeSO₄·7H₂O, showing typical XRD patterns of SO₄²⁻-type LDH (Supplementary Fig. 18b)³⁹.

As shown in Fig. 5a, the concentration of NO release can be controlled by adjusting the amount of NaNO₂-Mg/Al(3/1). Moreover, the duration of NO release is elongated using NaNO₂-Mg/Al(2/1). After the release of NO, the mixture changed its color from aqua-blue to brown, implying the oxidation of Fe²⁺ to Fe³⁺ (Fig. 5b). The NO generation was further confirmed by other methods, including gas-phase IR spectroscopy and chemiluminescence (Supplementary Figs. 7, 8, 19, and 20). Moreover, NO₂⁻-incorporated LDHs were stable at RT as long as they were kept isolated from air (Supplementary Fig. 17d).

Finally, we constructed a completely hand-operated (i.e., battery-free), disposable, and maintenance-free apparatus that can supply NO into the respirator (Fig. 5c). Wet air flow (~100 mL min⁻¹) was delivered to the mixture of NaNO₂-Mg/Al(3/1) and FeSO₄·7H₂O using a hand pump and humidifier (wet cotton). After passing through Mg(OH)₂, purified NO was mixed into the main air stream of the respirator. The NO concentration measured by the electrochemical sensor at the respirator was consistent with the result shown in Fig. 5a. Besides the merits described before, following are the notable technical features of our gas delivery system: (i) low risk of overdose (as far as LDH amount is adequate) and (ii) visibility of gas generation (through Fe³⁺ formation). In addition, if gas is released under N₂ flow, the obtained gas can be stored for a while without being oxidized.

In conclusion, solid materials that release p.p.m.-level H₂S and NO in response to aerial components (CO₂ and H₂O) are developed based on anion-exchange properties of LDHs at the solid-gas and solid-solid interfaces. The concentration and

duration of gas release are controllable by adjusting various factors (composition of materials, diffusion of gas molecules and anions, and chemical equilibrium). Not only protic gases (i.e., H₂S and HNO₂) but also nonprotic gases (i.e., NO and NO₂) can be released by combining anion-exchange and redox reactions. The concept is generally applicable and will guide a design of controlled release of various types of gases using a CO₂- and H₂O-affinitive confined interlayer space as a reaction vessel. A CO₂-stimulus is safe, free of cost, ubiquitous and nearly constant in concentration (~400 p.p.m.) on earth; hence, LDH-based gas-release materials is advantageous for operation under ambient air and will expand opportunities of utilizing functional gases in society, including application of physiologically active gases in developing countries and outside hospital.

Reporting summary. Further information on experimental design is available in the Nature Research Reporting Summary linked to this paper.

Data availability

The data that support the finding of this study are available from the corresponding authors upon reasonable request.

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Author contributions

S.I. and N.I. designed the research, performed experiments, and wrote the manuscript.

Competing interests

NIMS and Sumitomo Seika Chemicals, Co. Ltd filed a joint patent on H₂S-releasing materials, and NIMS solely filed a patent on NO_x-releasing materials and systems.

Additional information


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