Supplementary Materials

NMR Studies

a) $^1$H-NMR Study of Imine 3 Formation:

Experimental details:

Amine 2 (10 mg) in 580 $\mu$L of CDCl$_3$ were mixed with a stock solution of 2-pyridinecarboxaldehyde (20 $\mu$L, 22 $\mu$L of 2-pyridinecarboxaldehyde + 218 $\mu$L of CDCl$_3$) in an NMR tube. $^1$H-NMR spectra were recorded 3, 5, 15, 30, 45, 60, and 120 min after mixing the components.

Table S1. Conversion of imine 3 in CDCl$_3$ over time.

| Time after mixing (min) | Peak area (aldehyde proton) | % Aldehyde | Peak area (imine proton) | % Imine |
|------------------------|-----------------------------|------------|-------------------------|--------|
| 3                      | 0.8068                      | 80.68      | 0.1759                  | 17.59  |
| 5                      | 0.6398                      | 63.98      | 0.3626                  | 36.26  |
| 10                     | 0.4999                      | 49.99      | 0.4954                  | 49.54  |
| 15                     | 0.3643                      | 36.43      | 0.6348                  | 63.48  |
| 20                     | 0.2938                      | 29.38      | 0.7052                  | 70.52  |
| 30                     | 0.2241                      | 22.41      | 0.7770                  | 77.70  |
| 45                     | 0.1754                      | 17.54      | 0.8245                  | 82.45  |
| 60                     | 0.1413                      | 14.13      | 0.8436                  | 84.36  |
| 120                    | 0.1048                      | 10.48      | 0.8795                  | 87.95  |

Figure S1. $^1$H-NMR study of imine 3 formation in CDCl$_3$ over time.
b) $^1$H-NMR Study of Imine 3 Hydrolysis:

Experimental details:

Imine 3 (40.9 mol/mL) was dissolved in CDCl$_3$ (0.6 mL). Then a catalytic amount (<1 mg) of $p$-MeC$_6$H$_4$SO$_3$H was added. $^1$H-NMR spectra were recorded after 3, 5, 15, 30, 45, and 60 min.

**Figure S2.** $^1$H-NMR study of imine 3 hydrolysis by $p$-MeC$_6$H$_4$SO$_3$H in CDCl$_3$ over time.
c) $^1$H-NMR Dilution Study of Imine 3:

Figure S3. Aromatic region of the $^1$H-NMR spectra of imine 3 in CDCl$_3$ at a concentration of (a) $1.4 \times 10^{-3}$ M; (b) $2.7 \times 10^{-3}$ M; (c) $5.5 \times 10^{-3}$ M; (d) $1.1 \times 10^{-2}$ M; (e) $2.2 \times 10^{-2}$ M; (f) $2.8 \times 10^{-2}$ M.
d) VT $^1$H-NMR Spectra of Imine 3:

**Figure S4.** $^1$H-NMR spectra of imine 3 in DMSO-$d_6$ at non-gelling concentration (0.2% w/v, bottom spectrum) and as a DMSO-$d_6$ gel (2.5% w/v) at different temperatures (30–120 °C).

**Figure S5.** $^1$H-NMR subspectra of imine 3 in DMSO-$d_6$ at non-gelling concentration (0.2% w/v, bottom spectrum) and as a DMSO-$d_6$ gel (2.5% w/v) at different temperatures (30–120 °C).
e) VT $^1$H-NMR Spectra of Imine 3 and Pyrazinecarboxamide:

**Figure S6.** $^1$H-NMR spectra of gel of imine 3 and pyrazinecarboxamide (1:1) in DMSO-$d_6$ (2.8% w/v) at different temperatures (30–120 °C).

**Figure S7.** $^1$H-NMR subspectra of gel of imine 3 and pyrazinecarboxamide (1:1) in DMSO-$d_6$ (2.8% w/v) at different temperatures (30–120 °C).
e) $^{13}$C CPMAS NMR Spectra:

Figure S8. $^{13}$C-NMR spectrum of (a) imine 3, and $^{13}$C CPMAS NMR spectra of (b) xerogel of imine 3 from propan-1-ol; (c) xerogel of imine 3 from pentan-1-ol; (d) xerogel of imine 3 and pyrazinecarboxamide (1:1) from propan-1-ol; and (e) pyrazinecarboxamide recrystallized from propan-1-ol.

Note: Corresponding signals of the spectra of xerogels closely resemble to each other suggesting that imine 3 behaves very similarly in the xerogel state. The samples of the xerogels from propan-1-ol show relatively sharp signals indicating that they are more crystalline in nature than the sample of the xerogel from pentan-1-ol. Moreover, some signals reveal a double resonance pattern which means that the sample is either (i) a mixture of different polymorphic forms; or (ii) composed of a form having two non-equivalent molecules present in an asymmetric unit.

Photos of Gels

Figure S9. Photographs of gels (2 % w/v) of imine 3 in (a) propan-1-ol; (b) pentan-1-ol, and (c) DMSO; and of imine 3 and pyrazinecarboxamide (1:1) in (d) pentan-1-ol; and (e) DMSO.
Figure S10. Photographs of gel of imine 3 in propan-1-ol (2% w/v) after addition of 25 μL of 0.1 M aqueous solution of p-MeC₆H₄SO₃H.

Additional SEM Micrographs

Figure S11. SEM micrographs of xerogels of imine 3 in (a) pentan-1-ol and (d) DMSO; of imine 3+PC in (b) pentan-1-ol and (e) DMSO; and of imine 3+AP in (c) pentan-1-ol and (f) DMSO.

In Situ Gelation Study

Experimental details:

Total volume and the amount of imine 3 (experiments in Table S2) or amine 1 (experiments in Table S3) remained constant during the tests.

Table S2. Results of in situ gelation in propan-1-ol.

| Molar ratio (amine 1: aldehyde 2) | Gelation tests (after a heat/cool cycle) | Weight/volume percentage of in situ formed imine 3 | Total weight/volume percentage |
|----------------------------------|----------------------------------------|-----------------------------------------------|-------------------------------|
|                                  |                                        |                                               |                               |
| 3:1                              | P                                      | 2.00 %                                        | 5.42 %                        |
| 2:1                              | P                                      | 2.00 %                                        | 3.71 %                        |
| 1:1                              | P                                      | 2.00 %                                        | 2.00 %                        |
| 1:2                              | G                                      | 2.00 %                                        | 2.35 %                        |
| 1:3                              | G                                      | 2.00 %                                        | 2.70 %                        |
Table S3. Results of in situ gelation in propan-1-ol.

| Molar ratio (amine 1: aldehyde 2) | 1:0 | 1:0.2 | 1:0.4 | 1:0.6 | 1:0.8 | 1:0.9 | 1:1 | 1:2 | 1:3 |
|----------------------------------|-----|-------|-------|-------|-------|-------|-----|-----|-----|
| Gelation tests (after a heat/cool cycle) | S   | S     | P     | P     | P     | pG   | G   | G   | G   |
| Weight/volume percentage of in situ formed imine 3 | 0%  | 0.40% | 0.80% | 1.20% | 1.60% | 1.80% | 2.00% | 2.00% | 2.00% |
| Total weight/volume percentage | 1.71% | 1.77% | 1.82% | 1.88% | 1.94% | 1.97% | 2.00% | 2.35% | 2.70% |

Note: S – solution upon cooling, P – partly precipitate upon cooling, pG – partial gel, G – gel.

Drug Release Experiments

Figure S12. Schematic image of slow-release and acid-induced release of a drug.

Experimental details:

The gels of imine 3 and pyrazinecarboxamide (2.8% w/v), prepared in a 1:1 ratio in 0.5 mL of pentan-1-ol (nEC = 0.0195 mmol), were stabilised overnight. Then water (0.5 mL) either without or with p-toluenesulfonic acid (0.0053 mmol) was added. The samples stayed without any shaking or other type of disturbance. Water layers (0.4 mL) were separated off at certain times (after 0.5, 1, 2, 4 and 24 h), and after solvent evaporation in the open air, solid residues were dissolved in D2O (0.6 mL) and analysed by NMR with succinic acid (0.0042 mmol) as an internal standard. As control experiments (A and B), pyrazinecarboxamide (0.0195 mmol) was dissolved in pentan-1-ol (0.5 mL), and the samples were treated in the same way as the gel samples (adding of 0.5 mL of water either without or with 0.0053 mmol of p-toluenesulfonic acid, and then analysed by NMR with 0.0085 mmol of succinic acid as an internal standard). To check the drug release under non-calm conditions, the samples were treated by ultrasonic for 10 min and after one hour of standing without any additional disturbance, the water layers were analysed by NMR in the same way like in the other drug release experiments. The percentage of the released drug was calculated from the peak area of drug signals of a sample to the peak area of drug signals of a reference sample which was prepared by dissolving pyrazine-carboxamide (0.0195 mmol) in 0.6 mL of D2O with succinic acid (0.0085 mmol) as an internal standard. Results are summarised in Table S4.
Table S4 Results of drug release experiment.

| Reference |Peak area of drug signals|Peak area calculated for 0.0085 mmol of succinic acid|Peak area calculated for the whole sample (0.4 mL, > 0.5 mL)|Percent of released drug|Average % |
|-----------|-------------------------|-----------------------------------------------|--------------------------------------------------|------------------------|---------|
|Control experiment A (neutral conditions) | | | |
|0.5 h | 0.5856 | 0.6191 | 0.6165 | 0.5856 | 0.6191 | 0.6165 | 0.7320 | 0.7739 | 0.7706 | 40.9327 | 41.3793 | 41.2408 | 41.18 |
|1 h | 0.6023 | 0.6329 | 0.6350 | 0.6023 | 0.6329 | 0.6350 | 0.7529 | 0.7911 | 0.7938 | 42.1000 | 42.3016 | 42.4783 | 42.29 |
|2 h | 0.6341 | 0.6739 | 0.6747 | 0.6341 | 0.6739 | 0.6747 | 0.7926 | 0.8424 | 0.8434 | 44.3288 | 45.0420 | 45.1341 | 44.83 |
|4 h | 0.7315 | 0.7636 | 0.7671 | 0.7315 | 0.7636 | 0.7671 | 0.9144 | 0.9545 | 0.9589 | 51.1310 | 51.0373 | 51.3152 | 51.16 |
|24 h | 0.8082 | 0.8333 | 0.8265 | 0.8082 | 0.8333 | 0.8265 | 1.0103 | 1.0417 | 1.0332 | 56.4922 | 55.6973 | 55.2887 | 55.83 |
|shaking | 0.9410 | 1.0267 | 1.0382 | 0.9410 | 1.0267 | 1.0382 | 1.1763 | 1.2384 | 1.2978 | 65.7748 | 68.6223 | 69.4504 | 67.95 |

Control experiment B (acidic conditions) | | | |
|0.5 h | 0.5836 | 0.6164 | 0.6251 | 0.5836 | 0.6164 | 0.6251 | 0.7295 | 0.7706 | 0.7814 | 40.7901 | 41.2015 | 41.8147 | 41.27 |
|1 h | 0.6676 | 0.7042 | 0.7009 | 0.6676 | 0.7042 | 0.7009 | 0.8345 | 0.8802 | 0.8762 | 46.6616 | 47.0645 | 46.8800 | 46.87 |
|2 h | 0.6952 | 0.7307 | 0.7309 | 0.6952 | 0.7307 | 0.7309 | 0.8960 | 0.9134 | 0.9137 | 48.5908 | 48.8370 | 48.8949 | 48.77 |
|4 h | 0.8197 | 0.8597 | 0.8497 | 0.8197 | 0.8597 | 0.8497 | 1.0247 | 1.0746 | 1.0622 | 57.2974 | 57.4591 | 56.8420 | 57.20 |
|24 h | 0.8950 | 0.9400 | 0.9397 | 0.8950 | 0.9400 | 0.9397 | 1.1187 | 1.1750 | 1.1747 | 62.5566 | 62.8248 | 62.8626 | 62.75 |
|shaking | 0.9098 | 1.0546 | 1.0570 | 0.9098 | 1.0546 | 1.0570 | 1.2386 | 1.3182 | 1.3212 | 69.2585 | 70.4844 | 70.7053 | 70.15 |

Gel (neutral conditions) | | | |
|0.5 h | 0.7879 | 0.8119 | 0.8163 | 0.3940 | 0.4060 | 0.4082 | 0.4924 | 0.5074 | 0.5102 | 27.5366 | 27.1328 | 27.3032 | 27.32 |
|1 h | 0.9801 | 1.0548 | 1.0446 | 0.4901 | 0.5274 | 0.5223 | 0.6126 | 0.6593 | 0.6529 | 34.2539 | 35.2502 | 34.9393 | 34.81 |
|2 h | 1.0862 | 1.2139 | 1.1787 | 0.5431 | 0.6070 | 0.5894 | 0.6789 | 0.7587 | 0.7367 | 37.9620 | 40.5672 | 39.4246 | 39.32 |
|4 h | 1.2233 | 1.3161 | 1.3072 | 0.6117 | 0.6580 | 0.6536 | 0.7646 | 0.8225 | 0.8170 | 42.7536 | 43.9809 | 43.7226 | 43.49 |
|24 h | 1.3878 | 1.4876 | 1.4135 | 0.6939 | 0.7438 | 0.7068 | 0.8674 | 0.9298 | 0.8834 | 48.5028 | 49.7139 | 47.2780 | 48.50 |
|shaking | 1.5848 | 1.6963 | 1.7025 | 0.7294 | 0.8482 | 0.8513 | 0.9905 | 1.0602 | 1.0641 | 55.3878 | 56.6885 | 56.9444 | 56.34 |

Gel (acidic conditions) | | | |
|0.5 h | 1.1465 | 1.2065 | 1.2110 | 0.5733 | 0.6033 | 0.6055 | 0.7166 | 0.7541 | 0.7569 | 40.0695 | 40.3199 | 40.5049 | 40.30 |
|1 h | 1.2896 | 1.3815 | 1.3923 | 0.6448 | 0.6908 | 0.6962 | 0.8060 | 0.8634 | 0.8702 | 45.0705 | 46.1682 | 46.5690 | 45.94 |
|2 h | 1.3840 | 1.4553 | 1.4602 | 0.6620 | 0.7277 | 0.7301 | 0.8650 | 0.9096 | 0.9126 | 48.3700 | 48.6345 | 48.8400 | 48.61 |
|4 h | 1.5483 | 1.6310 | 1.6777 | 0.7742 | 0.8155 | 0.8389 | 0.9677 | 1.0194 | 1.0486 | 54.1121 | 54.5062 | 56.1149 | 54.91 |
|24 h | 1.7223 | 1.8358 | 1.8598 | 0.8612 | 0.9197 | 0.9299 | 1.0764 | 1.1474 | 1.1624 | 60.1933 | 61.3504 | 62.2057 | 61.25 |
|shaking | 1.9434 | 2.0451 | 2.0747 | 0.9717 | 1.0226 | 1.0374 | 1.2146 | 1.2782 | 1.2967 | 67.9207 | 68.3450 | 69.3935 | 68.55 |

Figure S12. 1H-NMR spectra of drug release experiment in D2O after 0.5, 1, 2, 4 and 24 h: (a) control experiment A (under neutral conditions); (b) control experiment B (under acidic conditions); (c) drug release from the gel under neutral conditions; (d) drug release from the gel under acidic conditions.