



HAL
open science

1,3-Acetonedicarboxylic Acid as a Simple Stimulus for Reversible Time-Controlled pH Modulation

Vincent Verdoot, Adrien Quintard

► **To cite this version:**

Vincent Verdoot, Adrien Quintard. 1,3-Acetonedicarboxylic Acid as a Simple Stimulus for Reversible Time-Controlled pH Modulation. *ChemSystemsChem*, 2024, 6 (1), pp.e202300037. 10.1002/syst.202300037 . hal-04426388

HAL Id: hal-04426388

<https://hal.science/hal-04426388>

Submitted on 30 Jan 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1,3-Acetonedicarboxylic Acid as a Simple Stimulus for Reversible Time-Controlled pH Modulation

Vincent Verdoot,^[b] Adrien Quintard^{*[a]}

[a] Dr. Adrien Quintard
Univ. Grenoble Alpes, CNRS, DCM, 38000 Grenoble, France
E-mail: adrien.quintard@univ-grenoble-alpes.fr

[b] Vincent Verdoot
Univ. Grenoble Alpes, CNRS, Grenoble INP*, LRP
38000 Grenoble, France

* Institute of Engineering Univ. Grenoble Alpes

Supporting information for this article is given via a link at the end of the document.

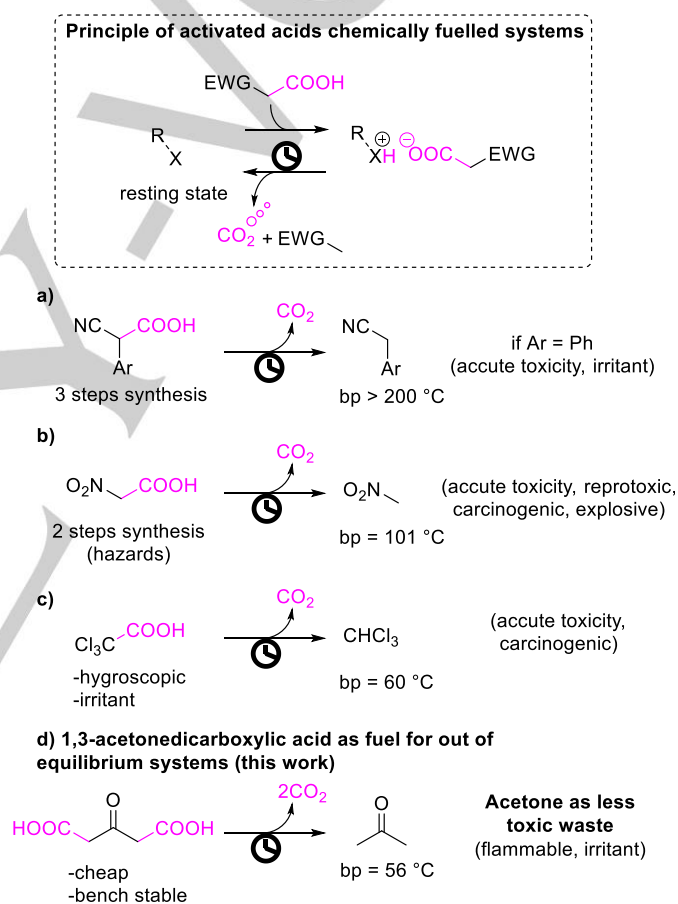
Abstract: Implementation of new activated carboxylic acids is crucial to switch reversibly chemical systems over time in a safer manner. By applying cheap 1,3-acetonedicarboxylic acid, the pH of aqueous solutions can be decreased before autonomously evolving over time back again to a higher value upon diacid decarboxylation. This decarboxylation can be catalysed by different species such as simple amines or simple metals such as iron and copper salts. This process generates 2 molecules of CO₂ and acetone as single waste, considerably decreasing the toxicity associated with such activated acids. The potential of this weak diacid was confirmed by reversibly disrupting a strong gel upon diacid addition and opens the way to the application in complex chemically fuelled systems.

Introduction

Ability to reversibly and autonomously change in properties is key for both natural biological systems and man-made machines. This requires an initial energy input to modify the system, followed by a reaction over time, ultimately allowing the system to autonomously return to its initial state.¹ Among the different fuels, chemical fuels, have the advantage of being transportable and applicable in different media. However, as a main limitation, they generate waste which can accumulate within the systems. In order to circumvent this issue, Nature has found complex solutions to recycle and eliminate all the waste generated.

In recent years, scientists have started working on the development of purely synthetic small chemical systems capable of changing properties in answer to a chemical stimuli and autonomously returning upon chemical reagent consumption to their initial state. Such properties were notably applied for simple switches, to complex motors or smart materials changing properties autonomously over time.²

Among the different chemical stimuli, the use of activated carboxylic acids enables to modulate easily system properties through changes in the relative acidity of the media (Scheme 1). Through such an approach, the reversible change in pH is obtained autonomously upon one single input while avoiding salts accumulation, as opposed to successive acid-base additions. These acids are based on carboxylic acids possessing adjacent electro-withdrawing groups.³ The acids can protonate a variety of basic functions (X), while the presence of the electron-withdrawing group favors decarboxylation, enabling the liberation of the initial bases with the concomitant release of CO₂ and of the protonated electron-withdrawing groups.



Scheme 1. Known activated carboxylic acids for chemical systems and 1,3-acetonedicarboxylic acid (drawn as the ketone form)

Different strong acids have been used for such purpose. The group of Di Stefano has notably used 2-cyano-2-arylpropanoic acids to fuel a variety of systems (Scheme 1a).⁴ The main advantage of these acids lies in the easily tunable kinetic of decarboxylation which depends on the nature of the aromatic group. As a limitation, these acids require three steps for their synthesis and generate non-volatile accumulating side-products. The same group reported that nitroacetic acid could act as an excellent chemical fuel notably in water but such approach was hampered by the increased hazards (Scheme 1b).⁵ Commercially available trichloroacetic acid is the most classically used acid (Scheme 1c).^{6,7} It has been used with success to fuel chemical

RESEARCH ARTICLE

systems based on rotaxanes, precipitation of supramolecular assemblies or time-dependent materials. However, this hygroscopic chemical liberates toxic chloroform upon decomposition, which prohibits its application as soon as biological environments are envisaged. It would thus be of great interest to find a simple alternative to these acids, that would be based on an easily handled cheap chemical, operable in water and liberating more volatile and less toxic waste. In addition, it would be further attractive to have a chemical whose kinetic of consumption could be modulated through the use of different catalysts and conditions.⁸

1,3-acetonedicarboxylic acid is a particular weaker diacid (pKa 3.1 and 3.77 in water).⁹ Its decarboxylation which can be mediated by different metal or organic catalysts liberates 2 molecules of CO₂ and volatile acetone.¹⁰ Since the pioneering tropinone synthesis by Robinson,¹¹ it was notably used with success notably by our group as an attractive acetone surrogate in different synthetic transformations upon activation by a suitable catalyst.¹² It is bio-based, coming from the decarboxylation of citric acid,¹³ and as a result represents a potential interesting alternative to classical

fuels for out of equilibrium chemical systems. Interestingly, in Nature acetoacetate decarboxylases are known to convert the parent acetoacetic acid into acetone, a secondary mechanism providing energy.¹⁴ However, the lack of stability of the mono-acid make it harder to handle and to use as potential fuel for synthetic out of equilibrium systems.

Herein, the potential of this diacid as an interesting chemical stimuli to induce a decrease in pH and an autonomous return to higher pH is described. It is a weaker acids than traditionally used acids presented in Scheme 1. As a result, the application of a weaker acid for time-controlled pH change would provide new opportunities to change pH of different systems with complementary properties.

Results and Discussion

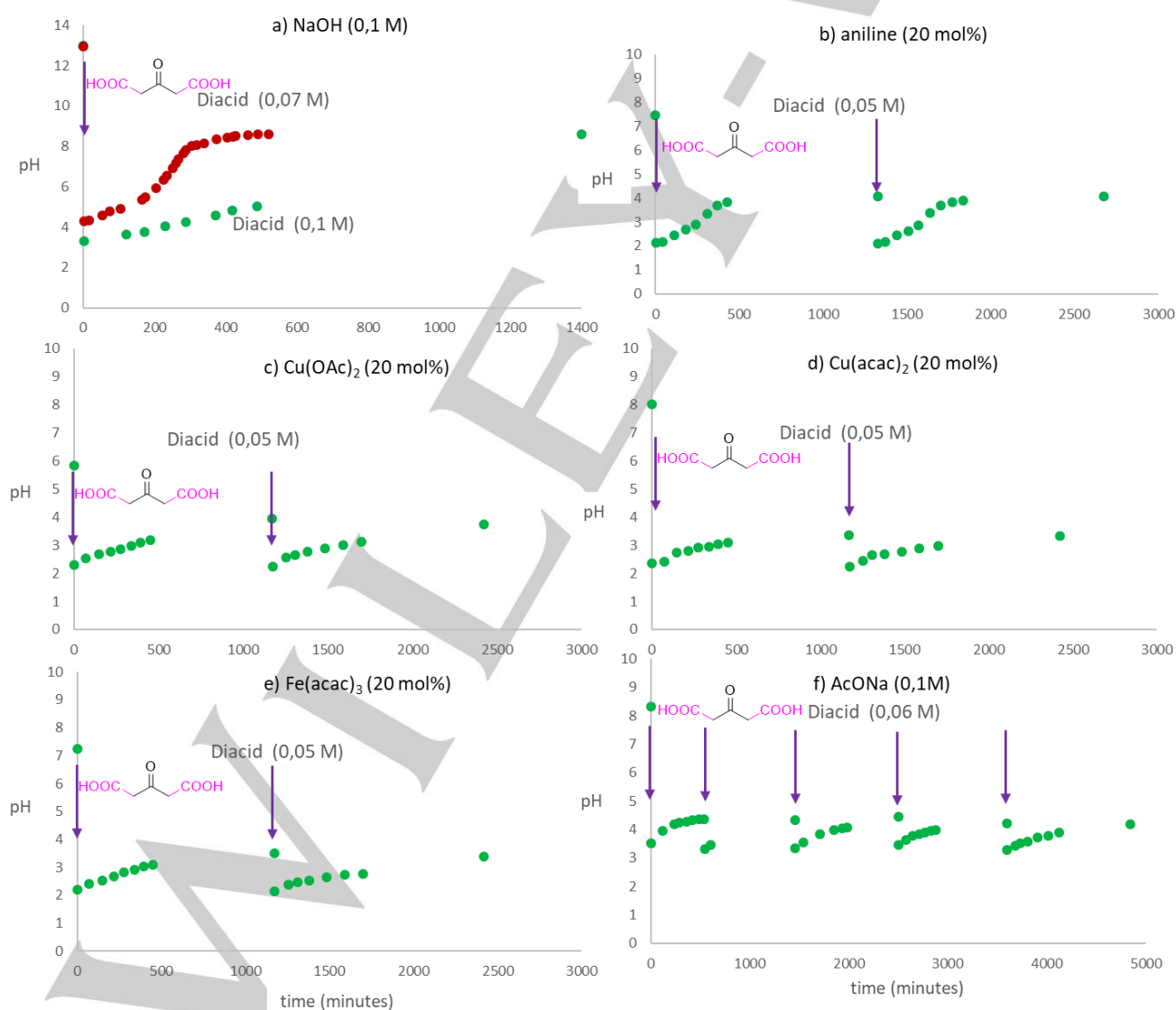


Figure 1. pH monitoring of the decomposition at 37°C of 1,3-acetonedicarboxylic acid in different solutions.

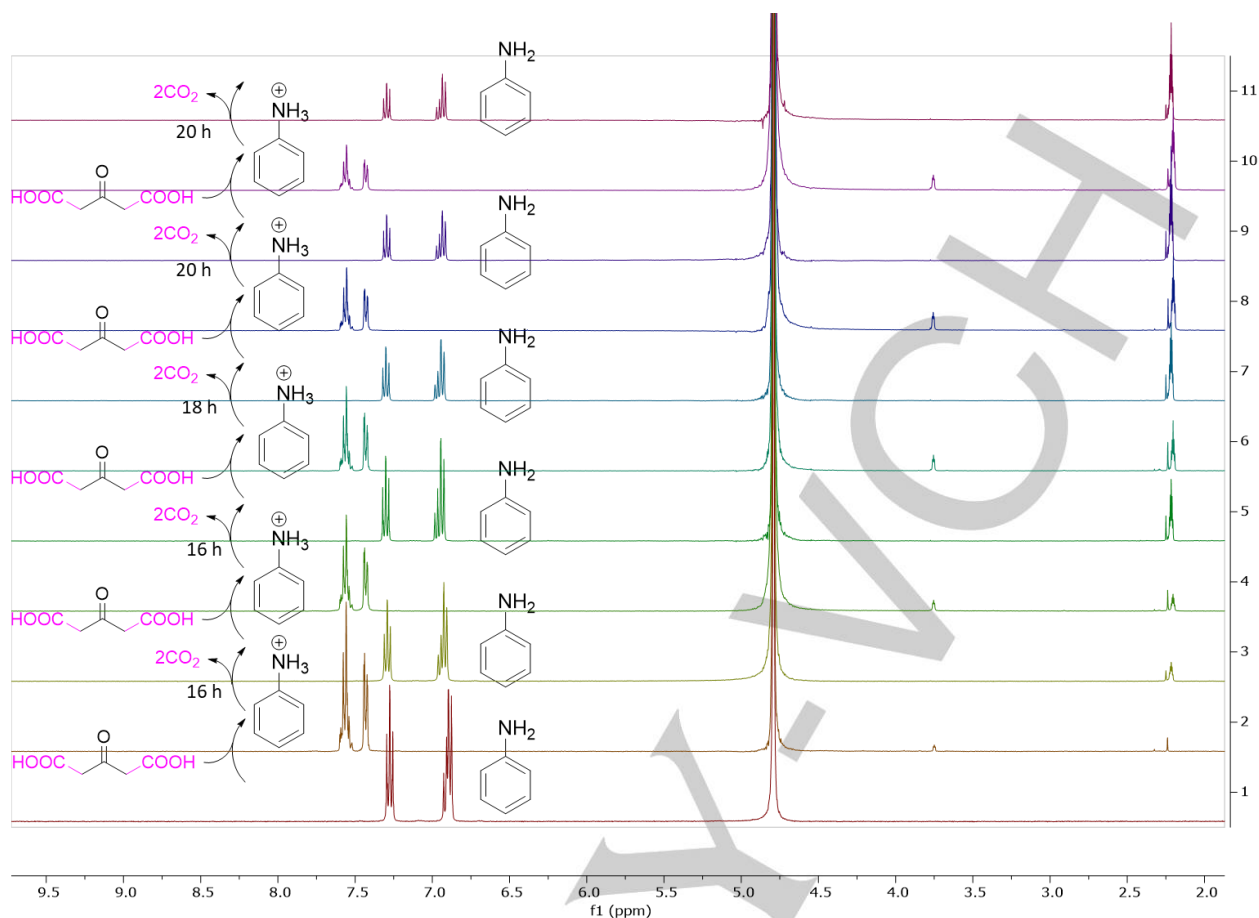
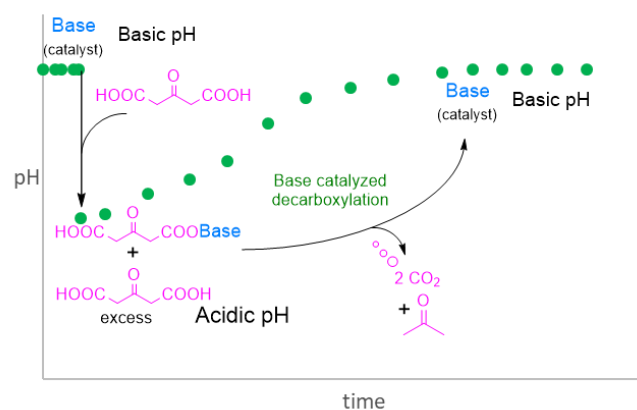


Figure 2. ^1H NMR monitoring of the decomposition of 1,3-acetonedicarboxylic acid catalyzed by aniline (20 mol%) in D_2O at 37°C .

At the onset, in order to probe the potential role of 1,3-acetonedicarboxylic acid as a time-dependent pH leveraging agent, we explored its decomposition using a wide array of reagents in order to probe their properties in the catalytic decarboxylation. 1,3-acetonedicarboxylic acid decarboxylation kinetic had been previously studied in aqueous buffered solutions, differing fundamentally from the present system leading to a change of the pH over time. Interestingly, a broad range of substances were able to catalyze the decarboxylation of 1,3-acetonedicarboxylic acid. (Figure 1). Addition of the diacid to the initial solutions, provided the expected pH drop, while subsequent decarboxylation, efficient at 37°C , slowly increased the pH over time. Of importance, one single equivalence point was observed, in agreement with the lower stability of the intermediate acetoacetic acid, rapidly decarboxylated under various conditions.^{10,15} This indicates that once the first decarboxylation occurs, the in-situ generated acetoacetic acid salt is rapidly decarboxylated.

In detail, adding 1 molar equivalent of diacid with respect to NaOH (Figure 1.a, red curve) did provide a jump from $\text{pH} = 12.95$ to $\text{pH} = 3.30$ before evolving overnight to a stable pH of 8.60. The observation of a final pH value higher than the initial one is due to the formation of hydrogen carbonate anions, generated upon reaction of the dissolved CO_2 with water.⁵ Decreasing the amount of diacid (Figure 1.a, green curve), the pH evolved upon diacid addition from 12.95 to 4.59 before increasing back again more rapidly upon 8 hours to $\text{pH} = 8.59$. In the absence of catalyst, the diacid was relatively stable at this temperature and only slowly

decomposed after several days (Figure S2). Aside from NaOH, several catalysts could also accelerate the decomposition of 1,3-acetonedicarboxylic acid, enabling evolution upon catalyst addition and decomposition over a range of pH (min $\text{pH} = 2.13$; max $\text{pH} = 4.44$).



Scheme 2. Representation of the pH evolution over time and of the chemical species present depending on the pH .

Aniline was more active in the decarboxylation of 1,3-acetonedicarboxylic acid, with only 20 mol% of this catalyst able to decompose the diacid almost completely after 500 minutes (Figure 1.b). From the initial solution at $\text{pH} 7.47$, upon addition of the diacid, the pH decreased to 2.16 before increasing back again

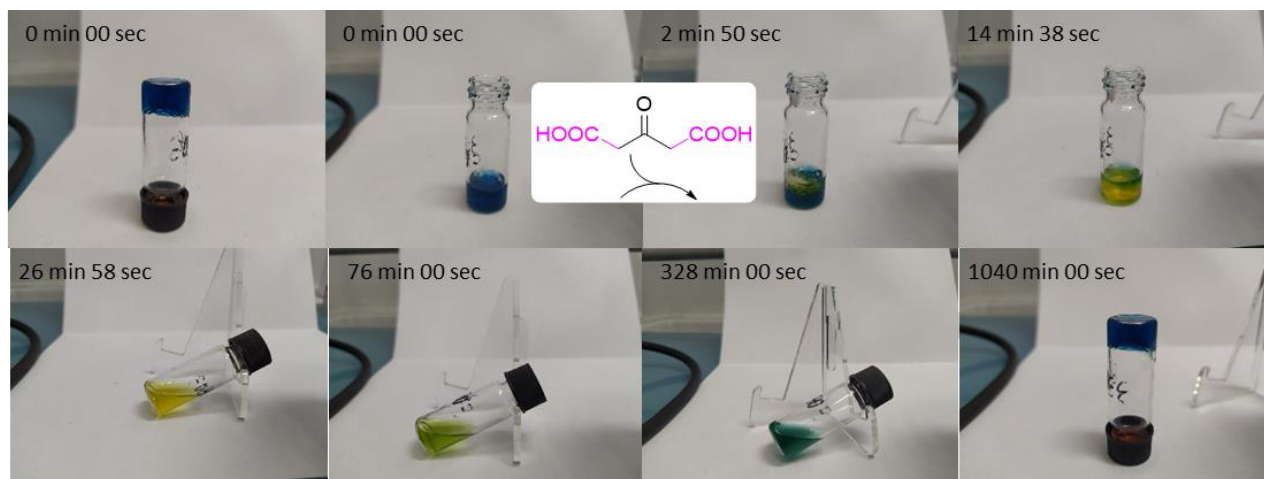


Figure 3. Images of the time-controlled reversible gelation by 1,3-acetonedicarboxylic acid. Diacid decarboxylation occurs at 37°C.

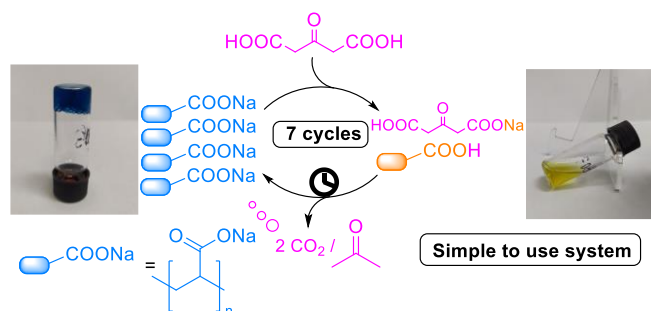
to 4.07. Upon another addition of diacid, the same pH evolution was observed again. Aside from this organocatalyst, several simple metal complexes could also catalyze the decomposition of 1,3-acetonedicarboxylic acid. $\text{Cu}(\text{Oac})_2$, $\text{Fe}(\text{acac})_2$ and $\text{Fe}(\text{acac})_3$ were all good catalysts providing similar decarboxylation profiles over two cycles with a complete decarboxylation occurring after around 16 hours (Figure 1.c-e). Finally, an excess of sodium acetate (AcONa) was also tested in the process in view of its potential role as catalyst for smart materials properties modulation (*vide infra*) (Figure 1.f). After a first cycle, similar shift of pH from 4.3 to 3.3 evolving back again to the initial value were observed over five cycles.

Altogether, these results confirm the behavior shown in Scheme 2. From the initial basic solution containing, addition of an excess of diacid protonates the small amount of base and the excess diacid decreases the pH to acidic values. Base-catalyzed diacid decarboxylation liberates acetone (*vide infra*) and CO_2 , leading back again upon time to the basic solution.

In order to gain more in-depth knowledge on the process, we then monitored by ^1H NMR the diacid consumption in the presence of aniline as catalyst over multiple cycles in D_2O (Figure 2). From the initial free amine (bottom), addition of an excess of 1,3-acetonedicarboxylic acid protonates the basic nitrogen leading to the anilinium salt, shifting downfield all aniline aromatic protons by 0.27 to 0.53 ppm. The diacid is almost not visible in the NMR range (0-12 ppm), due to the presence of the different delocalized enol forms in solution and to deuteration in D_2O .¹⁰ Upon aniline catalyzed decarboxylation, the free amine is liberated back again and most of the volatile acetone is evaporated outside of the system. The same cycle can be successfully repeated multiple times upon cycles initiated by the addition of the diacid and its subsequent decarboxylation. After several cycles, a small accumulation of acetone is observed (singlet at 2.22 ppm), not detrimental to the system since both aniline and anilinium ion are generated without any changes over the cycles. As a result, these results confirm the excellent behavior of the diacid which could be used to fuel a broad array of amine-based chemical out of equilibrium systems.²

With these experiments in hand, 1,3-acetonedicarboxylic acid was applied to modulate the properties of a material with a temporal control. The idea was to demonstrate this potential by

developing a system as easy to use as possible, from simple and cheap commercially available components, and displaying easily visible macroscopic properties. For this purpose, cheap sodium polyacrylate cross-linked,¹⁶ a common polymeric hydrogelator, was combined with the fueling by 1,3-acetonedicarboxylic acid (Scheme 3). At the initial state, the polymeric carboxylate anion would generate a strong gel, while in the presence of the diacid, protonation of the carboxylic acid would disassemble the gel. In order to better follow the pH transition in the system, bromocresol green, a colored pH indicator was added to the initial solution. From the initial blue gel (basic pH), addition of 1,3-acetonedicarboxylic acid acidifies the system providing a yellow solution (Figure 3). Upon diacid decarboxylation, occurring at 37°C, the polymeric free acid is recovered, the solution turns back again overtime from yellow to green then blue, generating again the strong gel. Gel formation and disruption was observed through the vial inversion method (a sample was considered as a gel if when the vial was inverted, no solution dropped). One can notice that upon gel destruction, the solution is not perfectly homogeneous and polymers residue corresponding to the gelator seem to precipitate upon diacid addition to the gel. This was confirmed when exploring the rheology of this system where the presence of the precipitating polymer prevented the observation of a solution at acidic pH. Interestingly, complementary to the previous systems using stronger acids,⁶ in the present system, application of a weaker acid implies a slower gel disruption kinetic, complete after around 25 minutes in the absence of any stirring of the system through the slow diffusion of the diacid (Figure 3). Finally, demonstrating the efficiency of the system, the gel disruption and reformation could be observed by the vial inversion method over 7 cycles upon 1,3-acetonedicarboxylic acid addition.



Scheme 3. Time-controlled gel disruption triggered by 1,3-acetonedicarboxylic acid

Conclusion

To conclude, 1,3-acetonedicarboxylic acid was shown to be a convenient molecule to induce time-controlled reversible changes in different chemical systems. It is cheap, widely available and less toxic than classical activated acids. Through the catalyzed decarboxylation, it can be easily decomposed liberating acetone and two molecules of CO_2 by triggering a reversible shift in pH over time. This decarboxylation can occur easily in the presence of a broad array of catalysts, from simple metal salts to amines. Demonstrating this potential, it was applied to reversibly disrupt a gel over time. Given these properties, this diacid should rapidly be applied in other complex time-controlled chemical systems.

Experimental Section

pH monitoring of the decomposition of 1,3-acetonedicarboxylic acid (0.1 M and 0.07 M) in 0.1 M NaOH at 37 °C. In a beaker placed in a 37°C bath, to a 20 mL NaOH solution (0.1 M), was added 1,3-acetonedicarboxylic acid (184.9 mg, 0.0014 mol, 0.07 M). The beaker was kept at 37°C and pH variation was recorded as a function of time by directly reading the pH value on the pH meter screen.

NMR monitoring of 1,3-acetonedicarboxylic acid decomposition: In a 5 mL vial, 2.0 mg of aniline (0.02 mmol, 20 mol%) were dissolved in 2.0 mL of D_2O . 14.6 mg of 1,3-acetonedicarboxylic acid (0.1 mmol, 1 equiv) were added and the reaction placed at 37°C. The reaction was monitored by reversibly transferring the vial content to a NMR tube and recording ^1H NMR spectra. Once all diacid consumed, the cycle was repeated by adding again 14.6±0.3 mg of 1,3-acetonedicarboxylic acid and heating at 37°C.

Gel evolution over 7 cycles: In a vial containing 1 mL of distilled water, 30.2 mg of sodium polyacrylate cross-linked were added and the mixture vigorously stirred for 5 seconds. A strong gel was rapidly formed within few seconds. Successive cycles of gel disruption and regeneration were performed by adding 40.3±2.0 mg of 1,3-acetonedicarboxylic acid (0.28 mmol), the vial stirred for 5 seconds and a solution formed within few minutes upon standing at room temperature. The solution was placed at 37°C leading back gradually to a strong gel after heating for 6-12 hours. Gel disruption was confirmed through the vial inversion method (a sample was considered as a gel if when the vial was inverted, no solution dropped). The gel disruption and reformation could be observed over 7 cycles upon 1,3-acetonedicarboxylic acid addition.

All experimental protocols, detailed analysis, pH-curves over time, other pictures of the material. This material is available free of charge in the

Supporting information. The data that support the findings of this study are available in the supplementary material of this article.

Acknowledgements

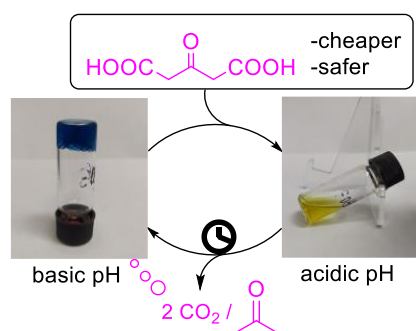
This work was supported by Université Grenoble-Alpes, the CNRS, the Agence Nationale de la Recherche (ANR) LabEx "Arcane" (ANR-11-LABX-0003-01). Eline Quintard is acknowledged for her help in initial gelation experiments. Dr. Jean-Luc Putaux and Dr. Christine Lancelon Pin from the CERMAV are gratefully acknowledge for their assistance on microscopic analysis.

Keywords: Chemical stimuli • time-controlled • gel • decarboxylation • catalysis

- [1] For general discussions, see: a) K. Das, L. Gabrielli, L. J. Prins, *Angew. Chem. Int. Ed.* **2021**, *60*, 20120-20143; b) S. Borsley, D. A. Leigh, B. M. W. Roberts, *Nature Chemistry*, **2022**, *14*, 728-738.
- [2] For reviews, see: a) S. A. P. van Rossum, M. Tena-Solsona, J. H. van Esch, R. Eelkema, J. Boekhoven, *Chem. Soc. Rev.* **2017**, *46*, 5519-5535; b) S. De, R. Klajn, *Adv. Mater.* **2018**, *30*, 1706750; c) N. Singh, G. J. M. Formon, S. De Piccoli, T. M. Hermans, *Adv. Mater.* **2020**, *32*, 1906834; d) G. Wang, S. Liu, *ChemSystemsChem*, **2020**, *2*, e1900046; e) Z. J. Leng, F. Peng, X. Hao, *ChemPlusChem*, **2020**, *85*, 1190-1199; f) B. Rieß, R. K. Grötsch, J. Boekhoven, *Chem*, **2020**, *6*, 552-578; g) S. Panja, D. J. Adams, *Chem. Soc. Rev.* **2021**, *50*, 5165; g) A. Sharko, D. Livitz, S. De Piccoli, K. J. M. Bishop, T. M. Hermans, *Chem. Rev.* **2022**, *122*, 11759-11777.
- [3] a) C. Biagini, S. Di Stefano, *Angew. Chem. Int. Ed.* **2020**, *59*, 8344 – 8354 ; b) D. Del Giudice, F. Fratello, C. Sappino, S. Di Stefano, *Eur. J. Org. Chem.* **2022**, e202200407; c) E. Olivieri, A. Quintard, *ACS Org. Inorg. Au* **2023**, *3*, 4–12; d) D. Del Giudice, S. Di Stefano, *Acc. Chem. Res.* **2023**, *56*, 889–899.
- [4] a) J. A. Berrocal, C. Biagini, L. Mandolini, S. Di Stefano, *Angew. Chem. Int. Ed.* **2016**, *55*, 6997-7001; b) C. Biagini, S. Albano, R. Caruso, L. Mandolini, J. A. Berrocal, S. Di Stefano, *Chem. Sci.* **2018**, *9*, 181-188; c) A. Ghosh, I. Paul, M. Adlung, C. Wickleder, M. Schmittel, *Org. Lett.* **2018**, *20*, 1046-1049; d) P. Franchi, C. Poderi, E. Mezzina, C. Biagini, S. Di Stefano, M. Lucarini, *J. Org. Chem.* **2019**, *84*, 9364–9368; e) D. Del Giudice, E. Spatola, R. Cacciapaglia, A. Casnati, L. Baldini, G. Ercolani, S. Di Stefano, *Chem. Eur. J.* **2020**, *26*, 14954-14962; f) I. Valiyev, A. Ghosh, I. Paula, M. Schmittel, *Chem. Commun.* **2022**, *58*, 1728-1731; g) A. Goswami, S. Saha, E. Elramadi, A. Ghosh, M. Schmittel, *J. Am. Chem. Soc.* **2021**, *143*, 14926–14935; h) A. Ghosh, I. Paul, *J. Am. Chem. Soc.* **2021**, *143*, 5319–5323; i) D. Del Giudice, M. Valentini, G. Melchiorre, E. Spatola, S. Di Stefano, *Chem. Eur. J.* **2022**, *28*, e202200685; j) D. Mondal, A. Ghosh, I. Paul, M. Schmittel, *Org. Lett.* **2022**, *24*, 69–73; k) V. Verman Rajasekaran, E. Elramadi, I. Valiyev, P. Howlader, M. Schmittel, *Chem. Commun.* **2023**, *59*, 3886-3889; l) D. Del Giudice, M. Valentini, C. Sappino, E. Spatola, A. Murrù, G. Ercolani, S. Di Stefano, *J. Org. Chem.* **2023**, *88*, 4379–4386.
- [5] a) D. Mariottini, D. Del Giudice, G. Ercolani, S. Di Stefano, F. Ricci, *F. Chem. Sci.* **2021**, *12*, 11735-11739; b) D. Del Giudice, E. Spatola, M. Valentini, C. Bombelli, G. Ercolani, S. Di Stefano, *Chem. Sci.* **2021**, *12*, 7460-7466.
- [6] a) Y. Abe, H. Okamura, K. Nakazono, Y. Koyama, S. Uchida, T. Takata, *Org. Lett.* **2012**, *14*, 4122-4125; b) N. Zhu, K. Nakazono, T. Takata, *Chem. Lett.* **2016**, *45*, 445–447; c) S. Erbas-Cakmak, S. D. P. Fielden, U. Karaca, D. A. Leigh, *Science* **2017**, *358*, 340–343; c) S. Choi, R. D. Mukhopadhyay, Y. Kim, I.-C. Hwang, W. Hwang, S. Kr Ghosh, K. Baek, K. Kim, *Angew. Chem. Int. Ed.* **2019**, *58*, 16850 –16853; d) C. Biagini, S. D. P. Fielden, D. A. Leigh, F. Schaufelberger, S. Di Stefano, D. Thomas, *Angew. Chem. Int. Ed.* **2019**, *58*, 9876-9880; e) E. Olivieri, G. Quintard, J.-V. Naubron, A. Quintard, *J. Am. Chem. Soc.* **2021**, *143*, 12650; f) O.

- Borodin, Y. Shchukin, C. C. Robertson, S. Richter, M. von Delius, *J. Am. Chem. Soc.* **2021**, *143*, 16448–16457; g) E. Spatola, F. Rispoli, D. Del Giudice, R. Cacciapaglia, A. Casnati, L. Marchiò, L. Baldini, S. Di Stefano, *Org. Biomol. Chem.* **2022**, *20*, 132–138; h) M. W. Wootten, S. Tshepelevitsh, I. Leito, J. Clayden, *Chem. Eur. J.* **2022**, e202202247; i) E. Olivieri, B. Gasch, G. Quintard, J.-V. Naubron, A. Quintard, *ACS Appl. Mater. Interfaces* **2022**, *14*, 24720; j) Y. Ren, R. Jamagne, D. J. Tetlow, D. A. Leigh, *Nature*, **2022**, *612*, 78–82; k) A. Thomas, B. Gasch, E. Olivieri, A. Quintard, *Beilstein J. Org. Chem.* **2022**, *18*, 225–231; l) D. Thomas, D. J. Tetlow, Y. Ren, S. Kassem, U. Karaca, D. A. Leigh, *Nature Nanotechnology*, **2022**, *17*, 701–707.
- [7] Tribromoacetic acid has also been applied, see: a) V. W. Liyana Gunawardana, T. J. Finnegan, C. E. Ward, C. E. Moore, J. D. Badjić, *Angew. Chem. Int. Ed.* **2022**, *61*, e202207418; b) G. Fusi, D. Del Giudice, O. Skarsetz, S. Di Stefano, A. Walther, *Adv. Mater.* **2023**, *35*, 2209870.
- [8] a) S. Amano, S. Borsley, D. A. Leigh, Z. Sun, *Nature Nanotechnology*, **2021**, *16*, 1057–1067; b) M. P. van der Helm, T. de Beun, R. Eelkema, *Chem. Sci.* **2021**, *12*, 4484–4493.
- [9] a) Larson, D. W.; Lister, M. W. *Can. J. Chem.* **1968**, *46*, 823–832; b) W. Hay, K. N. Leong, *J. Chem. Soc. A* **1971**, 3639–3647.
- [10] a) E. O. Wiig, *J. Phys. Chem.* **1928**, *32*, 961–981; b) B. R. Brown, M. A. D. Phil, *Q. Rev. Chem. Soc.* **1951**, *5*, 131–146; c) J. E. Prue, *J. Chem. Soc.* **1952**, 2331–2338; d) R. W. Hay, K. N. Leong, *J. Chem. Soc. A*, **1971**, 3639–3647; e) W. A. Jefferson, C. Hu, D. Song, H. He, J. Qu, *ACS Omega* **2017**, *2*, 6728–6740 and references cited herein.
- [11] R. Robinson, *J. Chem. Soc. Trans.* **1917**, *111*, 762–768.
- [12] a) A. Quintard, J. Rodriguez, *Chem. Commun.* **2015**, *51*, 9523–9526; b) A. Quintard, J. Rodriguez, *Chem. Eur. J.* **2015**, *21*, 14717–14722; c) A. Quintard, J. Rodriguez, *ACS Catal.* **2017**, *7*, 5513–5517.
- [13] R. Adams, H. M. Chiles and C. F. Rassweiler, *Org. Synth.* **1925**, *5*, 5.
- [14] D. T. Jones, D. R. Woods, *Microbiol. Rev.* **1986**, *50*, 484–524.
- [15] a) K. J. Pedersen, *J. Am. Chem. Soc.* **1929**, *51*, 2098–2107; b) R. W. Hay, M. A. Bond, *Australian Journal of Chemistry*, **1967**, *20*, 1823–1828; c) J. P. Guthrie, F. Jordan, *J. Am. Chem. Soc.* **1972**, *94*, 9136–9141.
- [16] a) M. Liu, T. Guo, *Journal of Applied Polymer Science*, **2001**, *82*, 1515–1520; b) F. Hua, M. Qian, *J. Mater. Sci.* **2001**, *36*, 731–738.

Entry for the Table of Contents



1,3-acetonedicarboxylic acid has been applied as a stimuli for reversible time-controlled pH modulation. It is cheaper and safer than commonly used reagents and enables to switch reversibly upon time the pH of a chemical system through its catalyzed decarboxylation. This was notably applied in the reversible disruption of an hydrogel.

Institute and/or researcher Twitter usernames: @adrien_quintard