Manipulation of an intramolecular NH · · · O hydrogen bond by photoswitching between stable *E*/*Z* isomers of the cinnamate framework†

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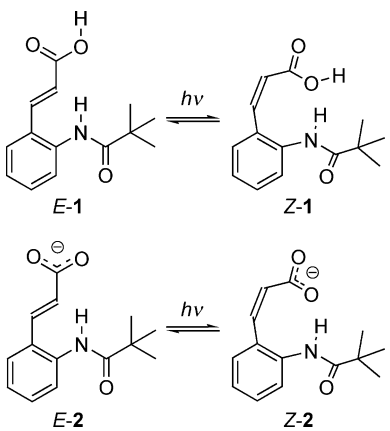
Novel carboxylic acid derivatives were synthesized, which allowed switching of the intramolecular distance between amide group and carboxylic oxygen atoms using *E* to *Z* photoisomerization of the cinnamate framework. An intramolecular NH · · · O hydrogen bond was formed in the *Z* carboxylate compound not only in solution but also in the solid state. The pK_a value of the carboxylic acid was lowered as a consequence of the *E*/*Z* photoisomerization.

Introduction

Hydrogen bonding plays an important role in expressing the function of proteins like native enzymes. It is thought that reactivity regulation is affected by switching of the hydrogen bond network around the active site.[1] In a previous study, we investigated the effect of the intramolecular NH · · · O hydrogen bond toward oxy anions, such as carboxylate and phenolate. We have proposed that the proximity of the amide NH group and the carboxylic oxygen atoms lowers the pK_a value of the corresponding acid by stabilizing the carboxylate through forming the intramolecular NH · · · O hydrogen bond.[2] Therefore, the switching of the intramolecular NH · · · O hydrogen bond by external stimulation (such as photoirradiation) is expected to realize the control of the pK_a value.

In this study, we designed novel carboxylic acid derivatives, which allow the switching of an intramolecular NH · · · O distance stimulated by light irradiation (Fig. 1). According to this strategy, photoirradiation stimulates the proximity of the amide NH and the carboxyl oxygen according to *E*/*Z* photoisomerization of a C=C double bond, which allows the intramolecular NH · · · O hydrogen bond to form at the carboxylate, and lowers the pK_a value of carboxylic acid. Photoisomerization, considered one of the most promising strategies for stimulating these compounds, effectively facilitates the control of molecular structures. There are many investigations using photoisomerization for photoswitching devices.[3] For example, the effects of intramolecular NH · · · N or NH · · · O hydrogen bonds in the *Z* form on *E*/*Z* photoisomerization of the C=C double bond,[4] as well as of the pK_a change of phenol or carboxylic acid derivatives by the switching of conjugation,[5] have also been investigated. However, to the best of our knowledge, no previous studies have attempted to control the character of carboxylates by switching an NH · · · O hydrogen bond. Previously, we examined the *E*/*Z* photoswitchable benzylideneaniline derivatives, which could switch the intramolecular distance between carboxylic oxygen atoms and the amide group, and revealed that the intramolecular NH · · · O hydrogen bond formed in the carboxylate is stronger than that in carboxylic acid.[6] However, because *Z*-benzylideneaniline derivatives are unstable at room temperature,[7] it was difficult to determine the acidity after photoisomerization. In this study, novel carboxylic acid derivatives (*E*-**1**/*Z*-**1**, *E*-**2**/*Z*-**2**), including the *E*/*Z* photoswitchable cinnamate frame, were synthesized (Scheme 1). High thermal stability of the *Z*-isomers of cinnamate enables us to isolate each conformation and to investigate detailed properties of them.



Scheme 1 Photoisomerization equilibria of cinnamic acid derivatives *E*-**1**/*Z*-**1** and *E*-**2**/*Z*-**2**.

Results and discussion

Synthesis

Scheme 2 shows the preparation of the photoswitching molecules. Cinnamic acid derivative *E*-**1** was synthesized by Heck reaction[8] of 2-pivalamidobromobenzene and ethyl propiolate. *E*-**2** was prepared through a counter-cation exchange reaction of *E*-**1**. *Z*-**2**

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† Electronic supplementary information (ESI) available: ^{1}H NMR spectra of the photostationary state of *E*/*Z*-**1** and -**2**, graphical data of the crystal packing structure of *E*-**1**, potentiometric titration curves of *E*-**1** and *Z*-**1**, 313/254 nm alternative photoisomerization data, and crystallographic data (CCDC reference numbers 603981 and 603982). See DOI: 10.1039/b719960k

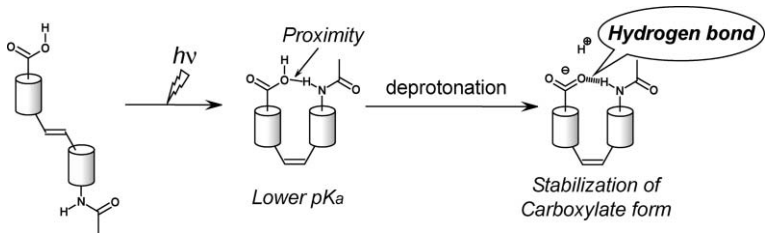
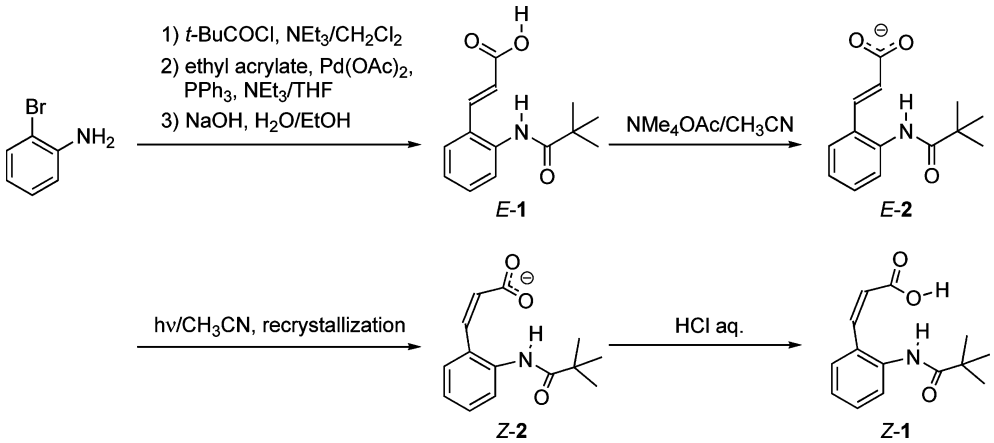


Fig. 1 Switching of an intramolecular NH · · · O hydrogen bond by *trans*/*cis* photoisomerization of an olefin.



Scheme 2 Synthesis of cinnamic acid derivatives *E*-**1**, *Z*-**1**, *E*-**2** and *Z*-**2**.

was isolated from the photoreaction mixture by recrystallization. *Z*-**1** was prepared through acidification of *Z*-**2**.

Direct photoisomerization of *E*-1 and *E*-2

Photoisomerization of *E*-**1** and *E*-**2** was traced by UV–visible (UV–vis) spectra. UV–vis spectrum changes of *E*-**1** and *E*-**2** caused by photoirradiation in dimethyl sulfoxide (DMSO) solution at 293 K are shown in Fig. 2. *E*-**1** and *E*-**2** were isomerized and reached the photostationary state (PSS) at 313 nm UV-light irradiation. Solid lines, corresponding to *E* isomers, are the spectra measured before irradiation, and broken lines represent the isolated pure *Z* isomers. The absorbance values of *E*-**1** and *E*-**2** are decreased in accordance with the two-state transition following irradiation (dotted lines), which indicates that only corresponding *Z* isomers are formed without any side reactions. The fraction of *Z* compounds in the PSS was determined from the integration ratio of ^{1}H NMR spectra. The *E* : *Z* ratio of the carboxylate is 7 : 93, whereas that of the carboxylic acid is 25 : 75 (supporting information).† It is difficult to cause the effective *Z* to *E* isomerization in DMSO solution. *Z* compounds are stable under heating, even at 363 K, and there is no suitable wavelength for irradiation at which *Z* compounds are preferentially excited. *Z*-**1** in chloroform solution allows about 10% of *E*/*Z* photocycling using alternate irradiation at 254 and 313 nm with decaying by photo decarbonation (supporting information).†

Molecular structures in solution

The solution structures of isolated *Z*-**1** and *Z*-**2** were determined by ^{1}H NMR spectra. The ^{1}H NMR spectra of *E*-**1**, *E*-**2**, *Z*-**1**, and *Z*-**2** in DMSO-d_6 at 303 K are shown in Fig. 3. All signals were assigned using the nuclear Overhauser effect (NOE) method and the decoupling method. *E*/*Z* configurations of these compounds were confirmed by the $^3J_{HH}$ value of the olefin protons. Generally speaking, the $^3J_{HH}$ coupling constant of olefin protons is about 15

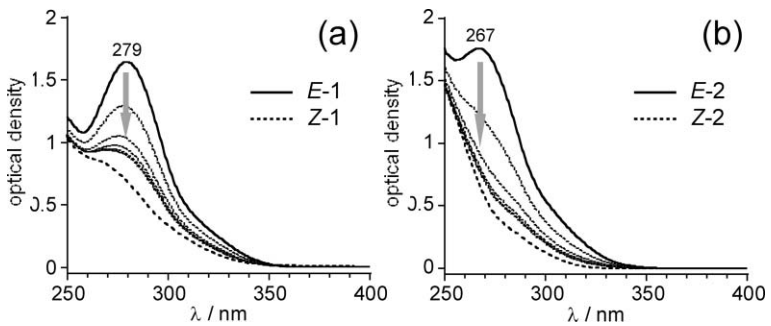


Fig. 2 Time course UV–vis spectra changes of *E*-**1** and *E*-**2** following photoirradiation at 313 nm, 1 mM in DMSO at 293 K.

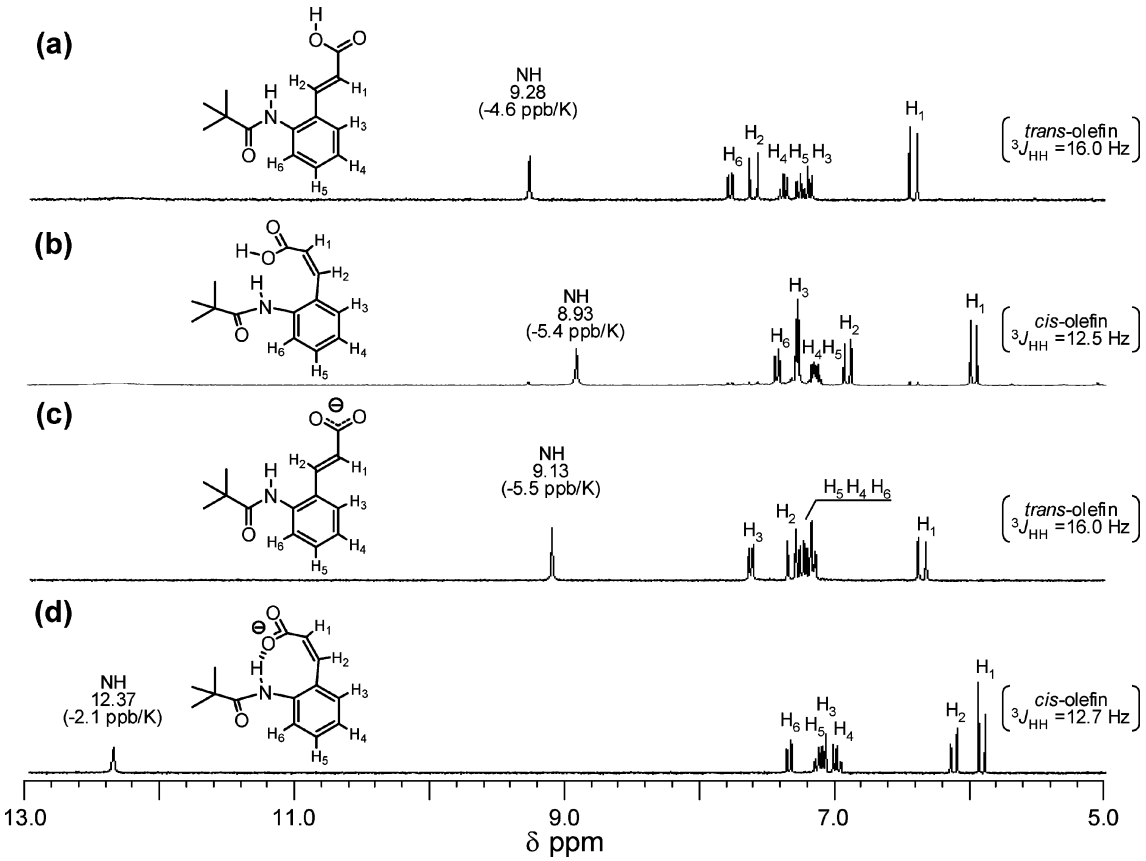


Fig. 3 ^{1}H NMR spectra of a) *E*-**1**, b) *Z*-**1**, c) *E*-**2** and d) *Z*-**2**, 5 mM in DMSO-d_6 at 303 K.

to 16 Hz in the *trans* position and about 12 to 13 Hz in the *cis* position. Observed $^3J_{HH}$ values of the olefin protons of *E*-**1** and *E*-**2** were 16.0 Hz, whereas those of *Z*-**1** and *Z*-**2** were 12.5 and 12.7 Hz, respectively. These observed $^3J_{HH}$ values coincide with the typical values of the *trans* and *cis* olefin protons. The configurations of the compounds before irradiation were confirmed as the *E* form, and the photoproducts were confirmed as the *Z* form.

The solution structures of the carboxylates are estimated based on the nuclear Overhauser enhancement spectroscopy (NOESY) spectra of *E*-**2** and *Z*-**2** (Fig. 4). An NOE correlation between NH and H2 was observed in *E*-**2**, but no NOE signal was observed between NH and H1 (Fig. 4a). This result indicates that the olefin moiety is likely to take the opposite direction to the amide moiety in *E*-**2** (s-*trans* form). In *Z*-**2**, an NOE correlation between H1 and

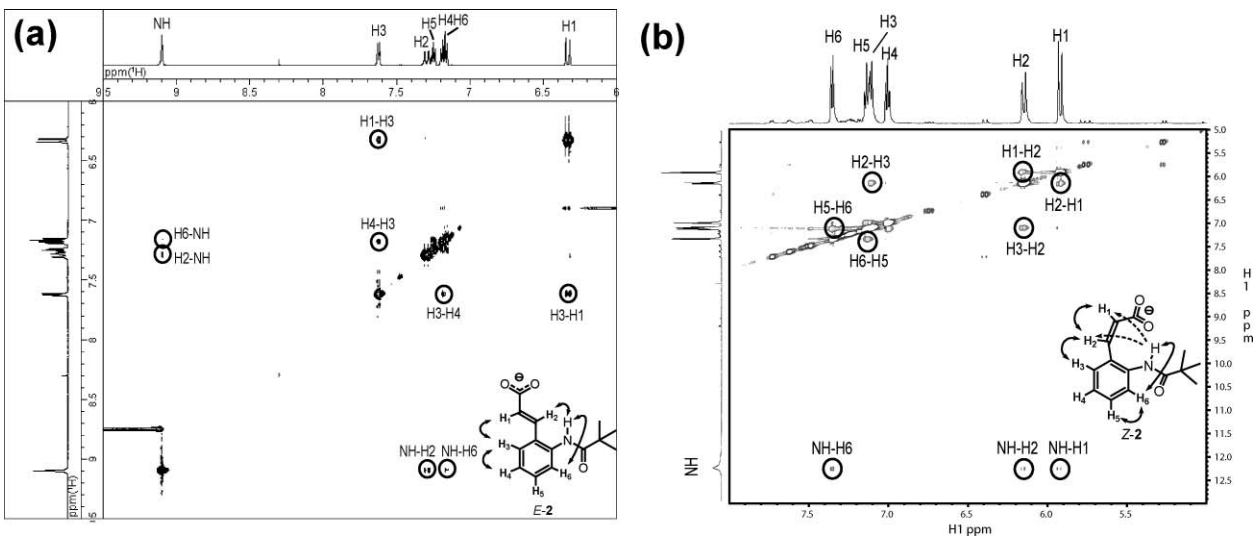


Fig. 4 NOESY spectra of a) *E*-**2** and b) *Z*-**2**, 5 mM in DMSO-d_6 at 303 K.

H2, which was not observed in *E*-**2**, was characteristically observed (Fig. 4b). This correlation confirms that the configuration of photoproduct *Z*-**2** was definitely in the *Z* form. The correlations of NH–H1 and NH–H2 in *Z*-**2** were weaker than those of NH–H6 or H2–H3. This result indicates that the olefin moiety in *Z*-**2** is likely to take the same direction as the amide side (s-*cis* form) and that the carboxylate is in close proximity to the amide moiety.

The chemical shifts of the amide NH signals of the *Z* isomers at 303 K were 8.93 ppm in *Z*-**1** and 12.37 ppm in *Z*-**2** (Fig. 3). The significant downfield shift ($\Delta\delta$ = 3.44 ppm) suggests that *Z*-**2** forms an NH $\cdots$ O hydrogen bond in DMSO-d_6 solution. The temperature dependency (range, 303–333 K) of the amide NH chemical shift of *Z*-**2** is –2.1 ppb K^{-1}, whereas that of *Z*-**1** is –5.4 ppb K^{-1}. The downfield shift and the decrease in the temperature coefficient of the NH proton suggest that *Z*-**2** forms an intramolecular NH $\cdots$ O hydrogen bond in DMSO-d_6 solution.

Molecular structures in solid state

To confirm the molecular structures in the solid state, X-ray crystallography was performed. The crystal structures of *E*-**1** and *Z*-**2** are shown in Fig. 5. Crystal data of *E*-**1** and *Z*-**2** are given in the experimental section. All non-hydrogen atoms were refined anisotropically. The coordinates of OH and NH protons were refined using fixed thermal factors, and the other protons were placed in calculated positions. The intramolecular O01 $\cdots$ N1 distance (4.854 Å) and the intermolecular O'03 $\cdots$ N1 distance (3.235[2] Å, O'03 indicates the O03 atom at the equivalent position [$x-1, y, z$]) of *E*-**1** are too long to form hydrogen bonds; the amide NH of *E*-**1** is free from any electrostatic interaction in the solid state. The intermolecular O02 $\cdots$ O'01 distance (2.632 Å, O'01 indicates the O01 atom at the equivalent position [$-x, -y+1, -z+1$]) of *E*-**1** permitted sufficient hydrogen bond formation; the dimerization of the carboxylic acid stabilizes the packing structure. The torsion angles of O02–C1–C2–C3 (−3.4[4]°) and C2–C3–C4–C5 (2.6[4]°) indicate that the cinnamic acid frame of *E*-**1** is almost in plane. However, the amide moiety is leaning away from this cinnamic acid plane (the torsion angle of C8–C9–N1–C10 is 36.0[3]°). These results inferred that the π-conjugation extends from the aromatic ring toward the carboxylic oxygen through the C=C double bond. In contrast, the distances of N1 $\cdots$ O1 (2.701[1] Å) and H1 $\cdots$ O1 (1.88[1] Å) of *Z*-**2** permitted sufficient hydrogen bond formation. The N1–H1–O1 angle of *Z*-**2** (154[1]°) is appropriate for hydrogen bonding. These results indicate that *Z*-**2** has an intramolecular NH $\cdots$ O hydrogen bond that forms an eight-membered ring structure in the solid state.

On the other hand, no intermolecular interactions (*e.g.*, hydrogen bonding) were detected in *Z*-**2**. Both of the C $\cdots$ O distances of carboxylate *Z*-**2**, C1 $\cdots$ O1 (1.255[2] Å) and C1 $\cdots$ O2 (1.246[2] Å), are virtually identical, whereas the C $\cdots$ O distances of carboxylic acid *Z*-**1** are C1 $\cdots$ O01 (1.281[2] Å) and C1 $\cdots$ O02 (1.262[2] Å). The torsion angles of O1–C1–C2–C3 (37.7[2]°), C2–C3–C4–C9 (−65.7[2]°), and C8–C9–N1–C10 (49.5[3]°) are so large that the π-conjugation of cinnamic acid extended in *E*-**1** is interrupted in *Z*-**2**. Solid Fourier transform infrared (FT-IR) spectra of the crystals of *E*-**1** and *Z*-**2** were measured to determine the existence of an intramolecular NH $\cdots$ O hydrogen bond in *Z*-**2**. *Z*-**2** exhibits the ν(NH) band at 3281 cm^{-1}, whereas the ν(NH) band appears at 3386 cm^{-1} in *E*-**1**. The low wavenumber shift of the ν(NH) band indicates the presence of a hydrogen bond in *Z*-**2**. These combined experimental results obtained by X-ray crystallography and FT-IR spectroscopy indicate that *Z*-**2** forms an intramolecular NH $\cdots$ O hydrogen bond in crystal.

Acidity change through photoisomerization

The pK_a values of *E*-**1** and *Z*-**1** were measured by potentiometric titration in a 10% Triton X-100 aqueous micellar solution at 298 K. The pK_a value of *Z*-**1** was 4.3, which was 0.5 units lower than that of *E*-**1** (pK_a = 4.8) (supporting information).† When the pK_a value was changed by photoisomerization, the pH value would also be changed. The pH change of *E*-**1** by 313 nm photoirradiation in Triton® X-100 aqueous micellar solution at 298 K is shown in Fig. 6. In conjugation with the *E* to *Z* photoisomerization, the pK_a value of the carboxylic acid was decreased, and the pH value also decreased from 3.51 to 3.29 (ΔpH = 0.22). This decrease in pH value corresponds to an increase in proton concentration (1.66 times higher).

To discuss the change in acidity in organic solvents, the counter-cation exchange reaction was examined. The difference of pK_a values in organic solvents is determined using the following method. If two acids, AH and BH, are in equilibrium (including the deprotonation process), the equilibrium equation is drawn in eqn (1), assuming that all anions have dissociated. The acid dissociation constants of AH and BH are defined as $K_a(1)$ and $K_a(2)$, respectively. The equilibrium constant, K_{eq} is indicated in

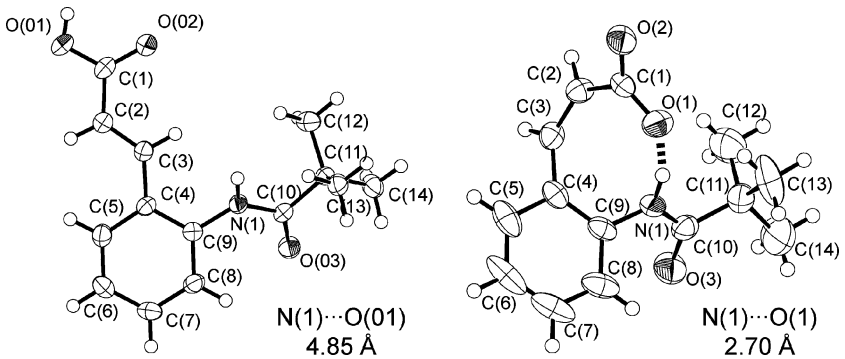


Fig. 5 Molecular structures of *E*-**1** (left) and *Z*-**2** (right), 50% probability.

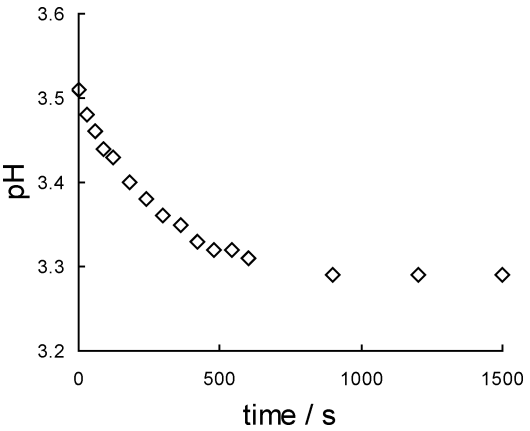


Fig. 6 pH change of 10 mM *E*-**1** by photoirradiation at 313 nm in 10% Triton® X-100 aqueous micellar solution at 278 K.

eqn (2), where K_{eq} is equal to the ratio of the acid dissociation constants of AH and BH. The ΔpK_a ($= \log K_{eq}$) value is calculated from $[A^-]/[AH]$ and $[BH]/[B^-]$.

$$AH + B^- \overset{K_{eq}}{\rightleftharpoons} A^- + BH \quad (1)$$

$$K_{eq} = \frac{[A^-][BH]}{[AH][B^-]} = \frac{[A^-][H^+]}{[AH]} \times \frac{[BH]}{[H^+][B^-]} = \frac{K_a(1)}{K_a(2)} \quad (2)$$

Carboxylic acid [AH] and carboxylate [B^-] are mixed in DMSO-d_6 solution, and the equilibrium constant is confirmed from the chemical shifts in the ^{1}H NMR spectra. Fig. 7 shows the ^{1}H NMR spectrum of the mixture of *E*-**1** and *Z*-**2** in DMSO-d_6 solution. Signals are shifted by mixing, which means that ion exchange reactions have occurred. The deprotonation ratio was estimated by comparing the authentic signals of the carboxylic acids and carboxylates. Using the chemical shift of the olefin protons (H2), it was possible to calculate the deprotonation ratio precisely because the signals were sharp and isolated. The chemical shift of the olefin proton of the *E* compound was closer to the chemical shift of carboxylic acid *E*-**1** than of carboxylate *E*-**2**, and that of he *Z* compound was closer to *Z*-**2** than *Z*-**1**. By comparing with the chemical shifts of isolated carboxylic acids and carboxylates, it is estimated that 83% of the *E* compound is protonated and that 90% of the *Z* compound is deprotonated. According to the results and eqn (2), the pK_a value of the *E* compound is 1.63 units lower than the pK_a value of the *Z* compound in DMSO solution.

Conclusion

In this work, photoswitching of an intramolecular NH···O hydrogen bond using *E* to *Z* photoisomerization was achieved. We synthesize the carboxylic acid *E*-**1**/*Z*-**1** and carboxylate *E*-**2**/*Z*-**2** derivatives, which have a photoinduced cinnamate frame, so as to switch the intramolecular distance between the amide NH and the carboxylic oxygen atoms using photoisomerization. *E* to *Z* photoisomerization was progressed using 313 nm UV light irradiation. Since the *Z* cinnamate compound is thermally stable, *Z*-**1** and *Z*-**2** are isolable from the mixture of photoisomers. *Z*-**2** forms an intramolecular NH···O hydrogen bond both in DMSO-d_6 solution and in the solid state. The pK_a value of *Z*-**1** was lower than that of *E*-**1**, not only in an aqueous micellar solution but also in DMSO solution. We propose that the intramolecular NH···O hydrogen bond formed in carboxylate *Z*-**2** encourages the deprotonation process and lowers the pK_a value of the corresponding carboxylic acid *Z*-**1**. Control of the pK_a of carboxylic acids by external stimulation will achieve the new functional small molecules which can control their nucleophilicity and exhibit regulated reactivity, like that of native enzymes.

Experimental

General procedures

All manipulations involving air- and moisture-sensitive compounds were carried out using standard Schlenk techniques under argon atmosphere. 2-Bromoaniline, 2,2-dimethylpropionyl chloride, triphenylphosphine, acrylic acid ethyl ester were purchased from Tokyo-Kasei Co. Palladium acetate, tetramethylammonium acetate were purchased from Aldrich Chemical Company, Inc. Dichloromethane was distilled over CaH_2. Tetrahydrofuran was distilled over CaH_2 and dried over Na. Ethanol and acetonitrile were distilled over CaH_2 and dried over molecular sieves (3 Å).

^{1}H NMR spectra (270 MHz) were measured on a JEOL JNM-GSX270 spectrometer. NOESY spectra were measured on a Varian UNITYplus 600 MHz spectrometer. The ^{1}H NMR spectra were referenced to the tetramethylsilane protons at δ 0.00. UV–vis spectra were measured on a Shimazu UV-3100PC spectrometer. Elemental analysis was performed at the Elemental Analysis Center, Faculty of Science, Osaka University. All melting points of the compounds were measured on a micro melting point apparatus of YANAGIMOTO Co. ESI-MS measurements were performed on a Finnigan MAT LCQ ion trap mass spectrometer. FT-IR spectra were measured on a JASCO FT/IR-8300 spectrometer,

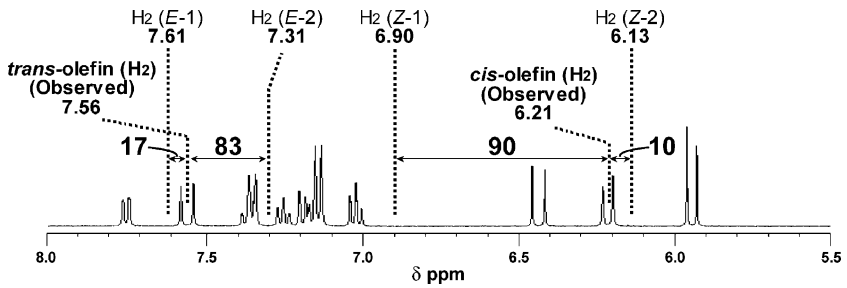


Fig. 7 ^{1}H NMR spectrum of the mixture of *E*-**1** and *Z*-**2** in DMSO-d_6 solution at 303 K.

and the solid FT-IR measurement was performed in a KBr glass cell with nujol. pK_a measurements were performed by potentiometric titration in 10 mM micellar solution at 298 K with a Metrohm 716 DMS titrino combined with a Metrohm 728 stirrer and a saturated calomel LL micro pH glass electrode. The saturated calomel micro glass electrode was calibrated with 0.05 M $KHC_8H_4O_4$ buffer (pH = 4.01) and 0.0025 M KH_2PO_4 buffer (pH = 6.86) at 298 K. The potentiometric titration was performed three times. pK_a values are estimated by an average value of each measurement.

Preparation of 2-pivaloylaminobromobenzene

To a solution of 2-bromoaniline (23.5 g, 0.138 mol) and triethylamine (25 mL, 0.18 mol) in distilled dichloromethane (150 mL) was added a solution of 2,2-dimethylpropionyl chloride (16 mL, 0.13 mol) in distilled dichloromethane (50 mL) solution in ice bath. A white solid precipitated from the orange solution. The mixture was stirred for 21 h at room temperature. The white solid was filtered off and the solution was evaporated to obtain a brown oil with a white powder. The mixture was dissolved in diethylether and washed with 2% aqueous hydrochloride, 4% aqueous sodium bicarbonate, water, and brine. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to obtain white crystals (31.2 g, 94%). Mp 60–63 °C; found: C, 51.59; H, 5.36; N, 5.57. Calc. for $C_{11}H_{14}BrNO$: C, 51.58; H, 5.51; N, 5.47%; δ_H(270 MHz; DMSO-d_6) 1.22 (s, 9H; *tert*-butyl), 7.13 (dt, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 7.37 (dt, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.5 Hz, 1H; aryl), 7.49 (dd, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 7.64 (dd, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.5 Hz, 1H; aryl), 8.92 ppm (s, 1H; NH); *m*/*z* (ESI) 277.9, 279.9 ([M + Na]$^+$ requires 278.0, 280.0).

Preparation of (*E*)-3-(2-pivaloylaminophenyl) acrylic acid ethyl ester

To a two-necked round bottom flask were added acrylic acid ethyl ester (4.35 mL, 4.00 g, 40.0 mmol), 2-pivaloylaminobromobenzene (5.12 g, 20.0 mmol), palladium acetate (0.133 g, 0.592 mmol), and triphenylphosphine (0.126 g, 0.48 mmol), which were suspended in triethylamine–tetrahydrofuran (13.2 : 10.0 mL, distilled). The mixture was refluxed for 63 h at 110 °C. The reaction was traced by TLC (ethyl acetate–hexane = 1 : 3; v/v) and by ^{1}H NMR spectrum. The mixture was concentrated to obtain black and white precipitates in orange oil. The mixture was suspended in tetrahydrofuran, and the catalyst was filtered off. The solvent was removed under reduced pressure to obtain orange oil. By TLC and by ^{1}H NMR spectrum, it was confirmed that the orange oil obtained was a mixture of the objective ((*E*)-3-(2-pivaloylaminophenyl) acrylic acid ethyl ester) and reactant (2-pivaloylaminobromobenzene). The crude products were used for the next reaction without further purification.

Preparation of (*E*)-3-(2-pivaloylaminophenyl) acrylic acid (*E*-1)

To a round bottom flask were added all the products obtained in the above reaction (the mixture of 2-pivaloylaminobromobenzene and (*E*)-3-(2-pivaloylaminophenyl) acrylic acid ethyl ester). The oil was dissolved in ethanol (40 mL). 1 M aqueous sodium hydroxide (40 mL, 0.040 mol) was added, and the solution turned to a white suspension. Ethanol (20 mL) was added to dissolve the precipitate. The solution was stirred for 24 h at room temperature. The reaction was traced by TLC (ethyl acetate–hexane = 1 : 3; v/v). The solution was concentrated to a white suspension. Saturated aqueous sodium bicarbonate was added and the suspension was extracted with diethylether. The organic layer was extracted with 4% aqueous sodium bicarbonate 3 times. The combined aqueous layer was acidified by ice-cooled aqueous sulfuric acid (pH 2–3). Oil-like white powder floated on a white suspension. The suspension was extracted with ethyl acetate, and the organic layer was washed with water and brine. The solution was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to obtain white powder (1.81 g, 36.6%). Mp 178–179 °C; found: C, 67.81; H, 6.88; N, 5.72. Calc. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66%); δ_H(270 MHz; DMSO-d_6) 1.24 (s, 9H; *tert*-butyl), 6.43 (d, ^3J(H,H) = 16.0 Hz, 1H; olefin), 7.19 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.2 Hz, 1H; aryl), 7.26 (dt, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.2 Hz, 1H; aryl), 7.39 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.6 Hz, 1H; aryl), 7.62 (d, ^3J(H,H) = 16.0 Hz, 1H; olefin), 7.79 (dd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.6 Hz, 1H; aryl), 9.28 (s, 1H; NH), 12.25 ppm (br s, 1H, COOH); *m*/*z* (ESI) 246.1 ([M − H]$^-$ requires 246.1), 270.3 ([M + Na]$^+$ requires 270.1).

Preparation of [tetramethylammonium](*E*)-3-(2-pivaloylaminophenyl) acrylate (*E*-2)

Tetramethylammonium acetate (53.8 mg, 0.404 mmol) was dissolved in distilled acetonitrile (2 mL). To the solution was added dropwise a solution of (*E*)-3-(2-pivaloylaminophenyl) acrylic acid (100 mg, 0.404 mmol) in distilled acetonitrile (4 mL) using a syringe. The solution was stirred for several hours, and the solvent was removed under reduced pressure to obtain an orange oil. Adding diethylether turned the oil to a gray powder. The supernatant solution was removed and the residue was dried under reduced pressure to obtain a gray powder. Yield was not confirmed. δ_H(270 MHz; DMSO-d_6) 1.24 (s, 9H; *tert*-butyl), 3.09 (s, 12H; NMe_4), 6.33 (d, ^3J(H,H) = 16.0 Hz, 1H; olefin), 7.17 (dt, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 7.18 (dt, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 7.24 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 7.30 (d, ^3J(H,H) = 16.0 Hz, 1H; olefin), 7.62 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.8 Hz, 1H; aryl), 9.10 ppm (s, 1H; NH).

Preparation of [tetramethylammonium](*Z*)-3-(2-pivaloylaminophenyl) acrylate (*Z*-2)

An acetonitrile solution of [tetramethylammonium](*E*)-3-(2-pivaloylaminophenyl) acrylate (100 mg) was irradiated by Xe/Hg arc lamp with 313 nm band pass filter for several hours. The fraction of *Z* isomers was confirmed by ^{1}H NMR spectrum to ensure the photoreaction had reached a photostationary state (>80% was *Z* isomer). The solvent was removed under reduced pressure. The obtained powder was recrystallized from hot acetonitrile. Colorless needle crystals were obtained. The crystals were washed with a little amount of acetonitrile and with diethylether. The yield was not certain. δ_H(270 MHz; DMSO-d_6) 1.17 (s, 9H; *tert*-butyl), 3.08 (s, 12H; NMe_4), 5.92 (d, ^3J(H,H) = 12.7 Hz, 1H; olefin), 6.13 (d, ^3J(H,H) = 12.7 Hz, 1H; olefin), 7.00 (dt, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.4 Hz, 1H; aryl), 7.09 (dd,

^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.4 Hz, 1H; aryl), 7.13 (dt, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.4 Hz, 1H; aryl), 7.36 (dd, ^3J(H,H) = 7.6 Hz, ^4J(H,H) = 1.4 Hz, 1H; aryl), 12.37 ppm (s, 1H; NH).

Preparation of (*E*)-3-(2-pivaloylaminophenyl) acrylic acid (*Z*-1)

The crystal of [tetramethylammonium](*Z*)-3-(2-pivaloylaminophenyl) acrylate (186.7 mg, 0.476 mmol) was suspended in ethyl acetate. The suspension was acidified by adding 2% aqueous hydrochloride, then the organic layer turned to a clear solution. The aqueous layer was extracted with ethyl acetate twice, and the combined organic layer was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to obtain a colorless oil. The oil was reprecipitated from diethylether–*n*-hexane to obtain a white powder. Yield 117.8 mg (81.8%). Mp 125 °C; found: C, 66.93; H, 6.99; N, 5.58. Calc. for $C_{14}H_{17}NO_3 \cdot (H_2O)_{0.2}$: C, 67.02; H, 6.99; N, 5.55%); δ_H(270 MHz; DMSO-d_6) 1.20 (s, 9H; *tert*-butyl), 5.98 (d, ^3J(H,H) = 12.5 Hz, 1H; olefin), 6.91 (d, ^3J(H,H) = 12.5 Hz, 1H; olefin), 7.14 (dt, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 1H; aryl), 7.17 (dt, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 1H; aryl), 7.29 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 1H; aryl), 7.44 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 1H; aryl), 8.94 (s, 1H; NH), 12.29 ppm (br s, 1H, COOH); *m*/*z* (ESI) 246.1 ([M − H]$^-$ requires 246.1), 270.1 ([M + Na]$^+$ requires 270.1).

Crystallographic data collections and structure determinations of *E*-1 and *Z*-2

Suitable single crystals of *E*-**1** and *Z*-**2** were mounted on a fine nylon loop with nujol and immediately frozen at 200 ± 1 K. All measurements were performed on a Rigaku RAXIS-RAPID Imaging Plate diffractometer with graphite monochromated MoKα radiation (λ = 0.71075 Å). The structures were solved by direct method (SIR 92)[9] and the subsequent refinements were performed using SHELXL-97[10] and teXsan crystallographic software package. All non-hydrogen atoms were refined anisotropically. The coordinates of OH and NH protons were refined using fixed thermal factors, and the other protons were placed in calculated positions. Crystal data for $C_{14}H_{17}NO_3$ (*E*-**1**): 0.30 × 0.20 × 0.10 mm^3, triclinic, $P\bar{1}$ (#2), a = 5.334(4) Å, b = 9.149(7) Å, c = 13.95(1) Å, α = 74.60(3)°, β = 80.12(3)°, γ = 82.77(2)°, V = 644(3) Å^3, Z = 2, ρ_{calcd} = 1.275 g cm^{-3}, μ(MoK$_\alpha$) = 0.89 cm^{-1}, M_w = 247.29. Total number of reflections measured 6238, unique reflections 2885 (R_{int} = 0.031), Final R indices: R_1 = 0.043, wR_2 = 0.120 for all data. GOF (F^2) = 0.86. Crystal data for $C_{18}H_{28}N_2O_3$ (*Z*-**2**): 0.30 × 0.20 × 0.20 mm^3, hexagonal, $P6_3$ (#173), a = 21.127(5) Å, c = 7.522(2) Å, V = 2907(4) Å^3, Z = 6, ρ_{calcd} = 1.098 g cm^{-3}, μ(MoK$_\alpha$) = 0.74 cm^{-1}, M_w = 320.43. Total number of reflections measured 27 898, unique reflections 27 887 (R_{int} = 0.039), Final R indices: R_1 = 0.041, wR_2 = 0.098 for all data. GOF (F^2) = 1.03. CCDC 603981 and CCDC 603982 contain the supplementary crystallographic data for this paper.†

UV-Light irradiation technique for UV–vis and ^{1}H NMR spectrum measurement

A Xe/Hg lamp (MUV-202U, Moritex Co.) was used for 313 nm UV-light irradiation. UV-Light was filtered through 6784-t01.uv1 (Asahi tech.) to pick out the 313 nm emission line of Hg gas. At TLC lamp was used for 254 nm UV-light irradiation, and UV-light was filtered through a solution filter (aqueous solution of $NiSO_4$, $CoSO_4$ and KI/I_2). The sample was dissolved in the degassed solvent under argon atmosphere and sealed in a quartz NMR tube or UV cell. The spectrum was measured before and after irradiation. During irradiation and spectrum measurements, the sample was always kept at the desired temperature.

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