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Three is company: Dual intramolecular hydrogen-bonding enabled carboxylic acid active in ring-opening polymerization

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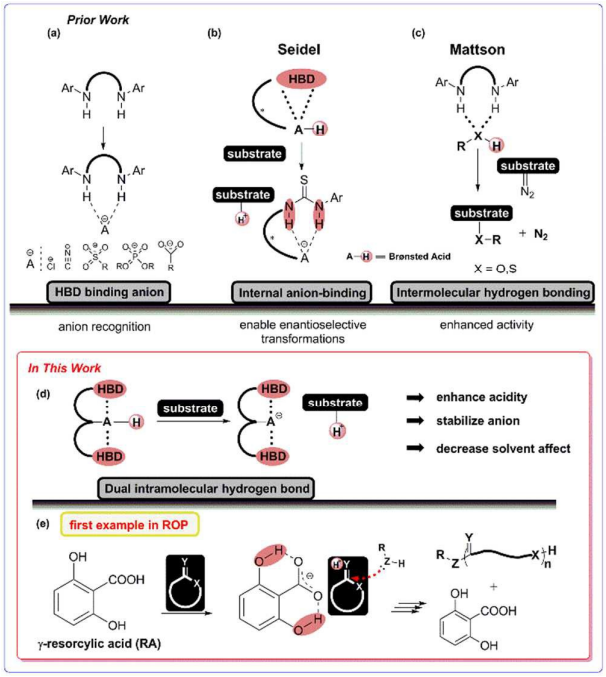
Hydrogen-bonding organocatalysis using (thio)urea and base received massive success. Intramolecular H-bonding (IMHB) assisted Brønsted acid (BA) catalysis, especially in polymerizations, was not explored. Here we suggested an IMHB–BA model in ring-opening polymerization (ROP) with γ-resorcylic acid (RA) as a representative catalyst, promoted ROPs of δ-valerolactone (VL) and ε-caprolactone (CL). The exceptional carboxylic acid RA showed efficient activation and precise control with high conversions (93–98 %), predicted molecular weights (from 3,090 to 13,000 g mol^{-1}), narrow dispersities (Đ 1.02–1.08), and nearly Poisson distributions (Đ ≤ 1.03) at higher molecular weights. A dual IMHB in RA was estimated by computational calculation, which predicted short H-bond lengths, near 180° bond angels, meant strong H-bonding. Cationic monomer activation mechanism was proposed and supported by NMR titration. The controlled/living nature of the ROPs was confirmed by kinetics and chain extension experiments. ^{1}H NMR, SEC, and MALDI-ToF MS analyses strongly indicated that the obtained PVL and PCL were exactly the designated ones. Synthesis of well-defined PVL-*b*-PCL and clickable end-functionalized PVLs verified again the catalytic ROPs were in controlled/living manner, and suggested the IMHB–BA catalysis to be a generally applicable method.

Introduction

Hydrogen bonding is key interaction in nature, which creates cooperative non-covalent networks support life and exerts efficient catalysis in (bio)molecular transformations.[1-2, 3] Catalysis by hydrogen bond donor (HBD) has emerged as a remarkable synthetic tool over the last decade.[4-6] The catalytic potential by dual H-bonding interactions,[7-9] prominently by the privileged (thio)urea and squaramide HBDs,[6, 10-17] received tremendous success. An HBD in cooperation with a Lewis/Brønsted base manifested a general bifunctional H-bonding catalysis, which received as "gold standard" in both asymmetric catalysis[10, 18, 19] and ring-opening polymerization (ROP).[20-24] In parallel with base promoted ROPs, Brønsted acid (BA) catalysis demonstrated to be complementary protocol in ROPs,[25-30] which showed unique capability in ROPs for base sensitive monomers.[31] However, strong to super strong BAs are usually required in these cationic ROPs, while the strong acidity may unfavourable to the tolerance of the catalysis and the polymerization. Indeed, mild and efficient BA catalysis in the cationic ROPs was in absence.



Scheme 1. Hydrogen-bond donor in organocatalysis: from anion recognition to intramolecular H-bonding assisted Brønsted acid organocatalysis in ROP.

HBD as receptor binding with (oxy)anion (**Scheme 1, a**), i.e. the conjugated–base of the counterpart Brønsted acid, is well known in (supra)molecular recognition[32-35] and crystal

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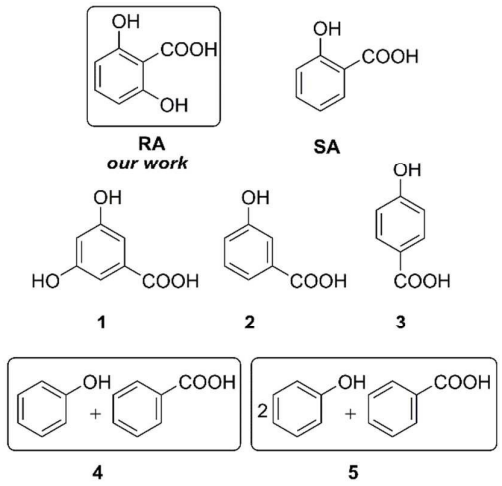
engineering.[36-39,] By contrast, HBD binding with BA itself is scarcely investigated.[40-42] Very recently, HBD and BA in co-catalysis or as promoters in small molecular transformations received a handful of reports.[43-48] Jacobsen pioneered the first chiral HBD and achiral BA co-catalysis in asymmetric synthesis.[43, 44] Seidel demonstrated the first intramolecular chiral HBD stabilized anion catalysis (**Scheme 1, b**) in Povarov[45] and Pictet-Spengler[47] reactions. In an insertion chemistry, Mattson proposed an HBD assisted acid amplification (**Scheme 1, c**).[46] We envisioned the possibility of a weak Brønsted acid assisted by intramolecular hydrogen-bonding (IMHB) would exhibit unusual activity and make a weak BA catalyzed ROPs feasible.

To validate our IMHB assisted BA (IMHB–BA) catalysis assumptions, we proposed a dual H-bonding assisted Brønsted acid model (**Scheme 1, d**), in which a weak BA (**A—H**) was appropriately embraced by two HBDs, each of the HBD was linked to the vicinity of the acidic site, which could facilitate associations amongst the HBDs and the Brønsted acid **A—H** or the (oxy)anion $\mathbf{A}^-$. The binding of HBDs with anion $\mathbf{A}^-$ promoted proton (H^+) releasing and protonating of the substrate, in this case, a cyclic monomer, and initiated its ROP (**Scheme 1, e**).

We were delighted to find γ-resorcylic acid (**Scheme 2, RA**), a natural, inexpensive, and commercially available dihydroxybenzoic acid, as model IMHB–BA, in which two hydroxyl groups (OH) were ideally located at the two *ortho*-positions to carboxylic on the benzene ring. This carboxylic acid showed unprecedented catalysis power in ROPs of δ-valerolactone (VL) and ε-caprolactone (CL) in solutions at room temperature. RA behaved an outlier, since simple carboxylic acid is known too weak to be active in ROPs, and hydroxyl acids including lactic and tartaric promoted ROPs of lactones at harsh conditions of high temperature (100 to 120 °C) in bulk by long time.[49-55] Control hydroxyl benzoic acids and phenol/benzoic acid pairs (**Scheme 2, SA, 1–5)** as congeners to RA were tested in the same ROPs and showed poor performance and negligible activities.



Scheme 2. γ-Resorcylic acid (**RA**) and congener hydroxybenzoic acids (**SA, 1-3**), and combinations of phenol and benzoic acid (**4** and **5**) evaluated as catalysts in the ROP of δ-valerolactone. Salicylic acid (**SA**), α-resorcylic acid (**1**), *m*-salicylic acid (**2**), *p*-salicylic acid (**3**), phenol/ benzoic acid = 1 / 1 (**4**), and phenol/ benzoic acid = 2 / 1 (**5**).

In this contribution, we described: (1) dual intramolecular H-bonding enabled carboxylic acid active in ROPs in solution at room temperature; (2) controlled/living nature of the ROPs catalyzed by γ-resorcylic acid was confirmed; (3) activated monomer mechanism was proposed and supported by NMR measurements, IR spectrum and computational calculations; (4) diblock co-polymers of δ-valerolactone and ε-caprolactone were synthesized by sequential feeding of the monomers in one-pot; (5) end-functionalized poly-δ-valerolactones were synthesized with clickable initiators.

Experimental section

Materials

δ-Valerolactone (VL; 99 %) and ε-caprolactone (CL; 99 %) were distilled over CaH_2 under reduced pressure in an inert environment. Dichloromethane (CH_2Cl_2; > 99 %; water content, < 0.001 %) was distilled over CaH_2 under an argon atmosphere, and further dried over 3 Å molecular sieve pellets for 48 h before use. Tetrahydrofuran (THF; > 99 %; water content, < 0.001 %) was purified by refluxing on sodium. Toluene (> 99 %; water content, < 0.001 %) was purified by refluxing on sodium. Acetonitrile (CH_3CN; > 99 %; water content, < 0.001 %) was dried over 3 Å molecular sieve pellets for 48 h. Benzyl alcohol (BnOH; Acros, 99 %) was refluxed over CaH_2 prior to distillation. All reagents and chemicals, except for the ones specified, were purchased from Sinopharm Chemical Reagent Co.

Characterizations

^{1}H NMR spectra were recorded on a Bruker-AV-400 spectrometer at 400 MHz in $CDCl_3$ to determine the monomer conversion and the number-average molecular weight ($M_{n,NMR}$). ^{13}C NMR spectra were measured at 100 MHz in DMSO to investigate the mechanism of the polymerizations.

Size exclusion chromatography (SEC) was performed at room temperature in tetrahydrofuran (THF) at a flow rate of 0.70 mL min^{-1}, by using a SSI 1500 pump equipped with a Waters Styragel HR 2.5 μm, 300 mm × 7.8 mm column, Wyatt Optilab rEX differential refractive index (DRI) detector with a 658 nm light source. The number-average molecular weight (M_n) and dispersities (M_w/M_n) were obtained by using a calibration with standard polystyrene samples.

Matrix assisted laser desorption/ionization time-of-flight mass spectra (MALDI-ToF-MS) were performed on a mass spectrometer (Ultraflextreme; Bruker Co.) with Smartbeam/Smartbeam II modified Nd: YGA laser. Mass spectra of five hundred shots were accumulated for the spectra at a 25 kV acceleration voltage. The polymer sample was dissolved in $CHCl_3$ at a concentration of 5 mg mL^{-1}, while the matrix 2,5-DHBA (2,5-dihydroxybenzoic acid) was dissolved in a solution of trifluoroacetic acid and acetonitrile with volume ratio of 70:30 in 10 μL water (1 %). Samples for the MALDI-ToF-MS were prepared by mixing the matrix and polymer solutions with the volume ratio of 1:1. The MALDI target was spotted with 1.0 μL of solution and allowed to air-dry.

The DFT calculations were performed using the GAUSSIAN 09 program with the 6-31^{++}G basis set, where Becke's three-parameter hybrid density functional[56] was used in combination with the Lee-Yang-Parr correlation functional (B3LYP)[57] to optimize the geometrical structures and to obtain relative energies.[58]

General procedure for polymerizations

All reactions were conducted under a dry nitrogen stream at room temperature. At first, VL (0.27 mL, 3.0 mmol, 30 equiv.) was dissolved in dichloromethane ($[VL]_0$ = 3.0 mol L^{-1}). Then, accurately weighted γ-resorcylic acid (0.0154 g, 0.10 mmol, 1.0 equiv.) as catalyst was added and dissolve completely. Third, the benzyl alcohol (10.3 μL, 0.10 mmol, 1.0 equiv.) as initiator was added. Finally, the mixture was stirred at room temperature under argon atmosphere. At the end of the polymerization, an excess of triethylamine was added to terminate the reaction. The reaction mixture was evaporated in reduced pressure. The obtained polymer was dissolved in a minimum amount of dichloromethane and separated out from cold methanol.

Block copolymerization of δ-valerolactone and ε-caprolactone

At first, VL (0.27 mL, 3.0 mmol, 30 equiv.) was dissolved in dichloromethane ($[VL]_0$ = 3.0 mol L^{-1}). Then, accurate weighted γ-resorcylic acid (0.0154 g, 0.10 mmol, 1.0 equiv.) as catalyst was added and dissolved completely. Third, the benzyl alcohol (10.3 μL, 0.10 mmol, 1.0 equiv.) as initiator was added. The mixture was stirred at room temperature under argon atmosphere. After 24 h, the CL (0.33 mL, 3.0 mmol, 30 equiv.) was added to start the block copolymerization to obtain poly(δ-valerolactone)-*block*-poly(ε-caprolactone) at the same conditions. At the end of the polymerization, an excess of triethylamine was added to terminate the reaction. Polymers were obtained by removing the solvents under vaccum evaporation. The raw polymer was dissolved in a minimum amount of dichloromethane and separated out from cold methanol.

Results and discussion

Polymerizations of δ-valerolactone and ε-caprolactone catalyzed by γ-resorcylic acid

γ-Resorcylic acid (RA) as an extraordinary carboxylic acid was demonstrated to be active, for the first time, in the ring-opening polymerizations of lactones in solution at room temperature. In order to verify the catalytic performance of RA in ROP, VL in dichloromethane ($[VL]_0$ = 3.0 mol L^{-1}) initiated with benzyl alcohol (BnOH) by RA catalysis at room temperature (25 °C) was evaluated (**Table 1**). Initially, ROP of VL at ratios of $[VL]_0/[BnOH]_0/[RA]$ = 30:1:1 (**Table 1, entry 1**) was carried out. The monomer conversion reached 94 % after 18 h by ^{1}H NMR. While, under the same conditions, RA can't catalyse the polymerization of lactide and trimethylene carbonate.

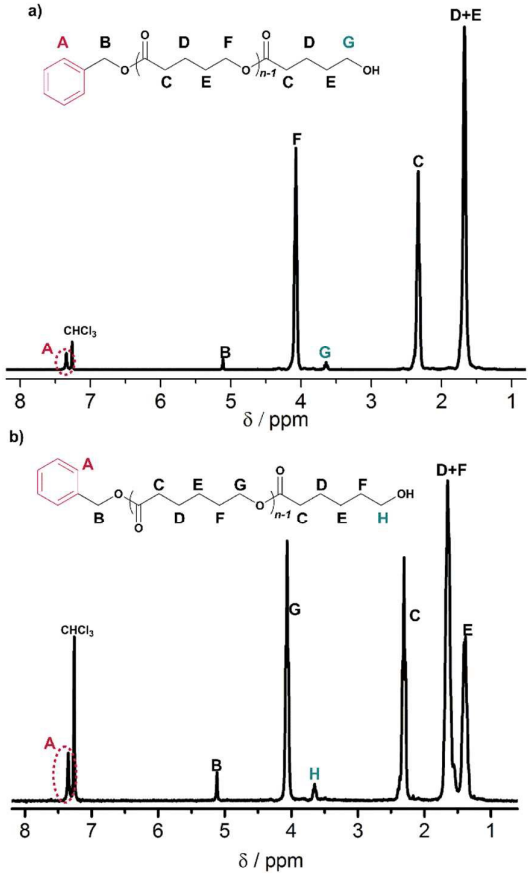


Figure 1. (a) ^{1}H NMR spectrum ($CDCl_3$, 400MHz) of poly(δ-valerolactone) ($[VL]_0/[BnOH]_0/[RA]$ = 30:1:1) and (b) ^{1}H NMR spectrum ($CDCl_3$, 400MHz) of poly(ε-caprolactone) ($[CL]_0/[BnOH]_0/[RA]$ = 30:1:1)

Table 1. ROP of δ-valerolactone (VL) and ε-caprolactone (CL) catalyzed by γ-resorcylic acid (RA) with benzyl alcohol (BnOH) as the initiator[a]

Entry	M	[M]/[I]	Time (h)	Conv.[b](%)	$M_{n,calcd}$[c] (g mol^{-1})	$M_{n,NMR}$[b] (g mol^{-1})	M_w/M_n[d]
1	VL	30	18	94	2920	3090	1.08
2	VL	50	18	93	4750	5030	1.03
3	VL	75	22	91	6930	7090	1.02
4	VL	100	24	80	8080	8090	1.02
5	VL	150	36	90	13600	13000	1.03
6	CL	30	24	93	3290	4320	1.06

[a] $[M]_0$ = 3.0 mol L^{-1}; room temperature. [b] Determined by ^{1}H NMR in $CDCl_3$. [c] Calculated from $([M]_0/[BnOH]_0)$ × conv. × (M_w of VL) + (M_w of BnOH). [d] Determined by SEC in THF using polystyrene standards.

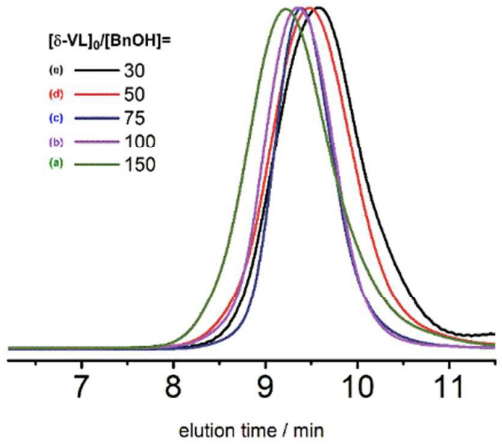


Figure 2. SEC traces of PVLs with various $[M]_0/[I]_0$ ratios of 30(a), 50(b), 75(c), 100(d), 150(e). Eluent, THF; flow rate, 0.7 mL min^{-1}

According to ^{1}H NMR spectrum of the obtained PVL (**Figure 1, a**), the peaks of the initiator (BnOH) residue were observed at the range of 7.23–7.39 and 5.12 ppms; the peaks for the repeated unit (VL) in the polymer chain appeared at 2.31, 1.62–1.7, 1.39, 4.05 and 3.65 ppms, respectively. These results demonstrated that the obtained PVL was initiated from BnOH. Similar catalysis by RA was investigate in ROP of CL under the same conditions with CL in dichloromethane ($[CL]_0$ = 3.0 mol L^{-1}) at room temperature (25 °C) by ratios of $[CL]_0/[BnOH]_0/[RA]$ = 30:1:1 (**Table 1, entry 6**). The CL monomer conversion was 93 % after 24 h, which was determined by ^{1}H NMR spectrum, and the structure of the PCL was similarly identified (**Figure 1, b**). The consumption rate of VL was faster than that of CL, which agreed with the reported systems[59, 60] for the cationic polymerizations of VL and CL.

In order to confirm the controlled/living nature of the polymerizations by RA, we carried out ROPs of VL by varying the $[VL]_0/[BnOH]_0$ ratios from 30 to 150 (**Table1, entries 1–5**). The results showed that the obtained PVLs of predicted $M_{n,NMR}$ agreed perfectly with the calculated ones by the initial ratios of $[VL]_0/[BnOH]_0$ and the corresponding monomer conversions. Their distributions were narrow, as shown in **Figure 2**, and the dispersities (M_w/M_n) were very low in the range of 1.02–1.08. With the ratios of $[VL]_0/[BnOH]_0$ increasing from 50 to 150, all the M_w/M_n dispersities were kept below an ideal value (≤ 1.03) approaching Poisson distributions,[61, 62] e.g. the M_w/M_n value was 1.03 for the PVL with a $M_{n,NMR}$ of 13,000 g mol^{-1} (**Table1, entry 5**), this was spectacular in cationic ROPs.

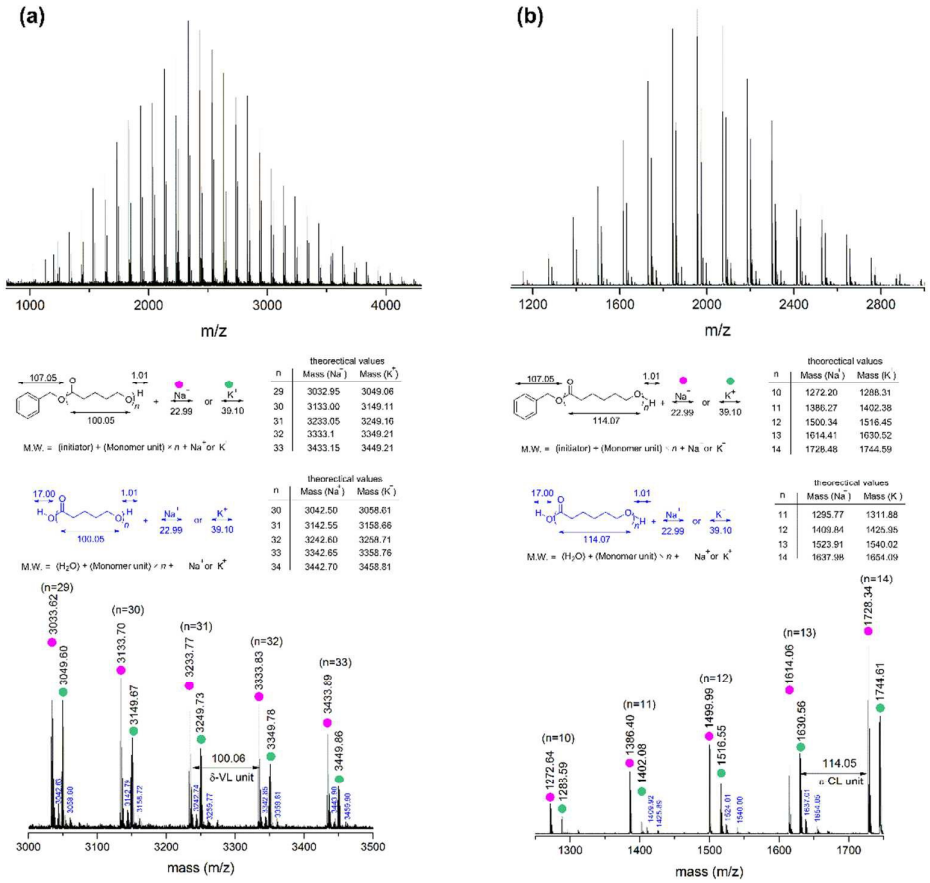


Figure 3. (a) MALDI-ToF MS spectra of the obtained PVL ($[VL]_0/[BnOH]_0/[RA]$ = 50:1:1, conversion = 78 %, $M_{n,NMR}$ = 3440 g mol^{-1}, M_w/M_n= 1.06), (b) MALDI-ToF MS spectra of the obtained PCL ($[CL]_0/[BnOH]_0/[RA]$ = 50:1:1, conversion = 46 %, $M_{n,NMR}$ = 1620 g mol^{-1}, M_w/M_n = 1.07)

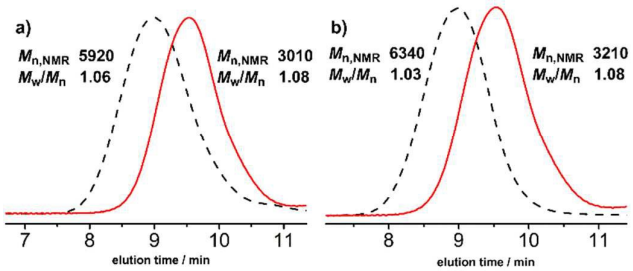


Figure 4. (a) SEC traces of the first PVL sample (solid line) and post-polymerization PVL sample (dashed line). (b) SEC traces of poly(δ-valerolactone) (PVL; solid line) and poly(δ-valerolactone)-block- poly(ε-caprolactone) (PVL-*b*-PCL; dashed line)

The chain extension experiment further supported the controlled/living nature of the RA-catalyzed ROPs of VL. In SEC traces for chain extension experiments (**Figure 4, a**), the first polymerization proceeded with $[VL]_0/[BnOH]_0$ = 30:1 in dichloromethane at room temperature without quenching, the monomer conversion reached 94 % with $M_{n.NMR}$ = 3,010 g mol^{-1} and M_w/M_n = 1.08 after 18 h. Additional VL (30 equiv.) was added to start the second polymerization for further 24 h, obtaining PVL with $M_{n,NMR}$ = 5,920 g mol^{-1} and M_w/M_n = 1.06, indicating the chain end group of PVL truly possessed a living nature.

Direct evidence that BnOH exclusively initiated the RA-catalyzed ROPs of VL and CL was provided by MALDI-ToF MS measurements (**Figure 3**). For example, from the MALDI-ToF MS spectrum of PVL (**Figure 3, a**), two main series of peaks perfectly agreed with the theoretical molecular weights of PVL possessing the residual BnOH and the hydroxyl chain end. The mass differences between the neighbouring peaks were identical to the molecular weight of the VL unit. Such as, for the 29-mer, the measured values with K^+ 3049.60 and with Na^+ 3033.62 corresponded to the calculated values with the respective potassium and sodium ions (K^+ 3049.06 and Na^+ 3032.95) (**Figure 3, a**). In view of our laboratory facilities, another two series of unexpected peaks (initiated by H_2O) ionized by potassium and sodium ion, respectively, were also observed in the spectrum.[24, 59, 60, 63] Interestingly, measured values of peaks (initiated by H_2O) fairly agreed with the calculated values, and the spacing of two neighboring peaks closely agreed with the molecular weight of a VL unit, which strongly indicated that H_2O could act as efficient initiator.The above discussions applied also to the MALDI-ToF MS analysis of PCL corresponding to linear polymer chains initiated by BnOH (**Figure 3, b**).

To exploit the living character of the propagating PVL chain, copolymerization of VL with CL to produce PVL-*b*-PCL by one-pot, sequential feeding of the two monomer lactones were demonstrated with $[VL]_0/[BnOH]_0/[RA]$ = 30:1:1 in the first polymerization. After VL was consumed, CL (30 equiv.) was added for the second polymerization. The obtained copolymers were determined by ^{1}H NMR, ^{13}C NMR spectra and DSC traces (**see Figure S1, S2 and S3**). The SEC traces illustrated that the molecular weights of the obtained PVL and its corresponding PVL-*b*-PCL shifted from 3,210 to 6,340 g mol^{-1}, and the dispersities were obviously narrowed from 1.08 to 1.03 (**Figure 4, b**). All these results indicated that RA was an efficient catalyst in polymerizations towards well-defined diblock copolymers of VL with CL.

Solvent effect on polymerizations δ-valerolactone catalyzed by γ-resorcylic acid

Hydrogen bonding in organocatalysis is very sensitive to solvents.[64-66] However, an H-bonding relevant process is arguably not susceptible to solvent effect when IMHB is predominant.[67-69] In our case, the two *ortho*-hydroxyls to the carboxylic in RA ideally formed two six-membered rings fused by dual intramolecular H-bonding, which will be estimated by computational calculations further (*vide infra*).

Here we inspected the advantages of the IMHB by two hydroxyls in assistance of carboxylic in RA by using an array of common solvents in ROPs to probe the effect on polymerizations of VL (**Table 2**). In less polar solvents of negligible propensity as H-bond acceptor (**Table 2, entries 1 and 2**), high conversions and narrow dispersities were recorded. In strong H-bond acceptor solvent tetrahydrofuran (**Table 2, entry 3**), almost quantitative conversion (98 %) and nearly Poisson distribution (Đ = 1.06) were received. Polar solvent acetonitrile (**Table 2, entry 4**) showed somewhat slow rate, however, predicted molecular weights and excellent dispersities (1.06) implied that it was in a controlled/living manner.

The latter two cases demonstrated the unusual catalytic power of RA in cationic ROPs, in which strong intramolecular hydrogen-bonding circumvented the competition from solvent molecules and kept the IMHB undisturbed. On the contrary, intermolecular hydrogen-bonding catalysis often seriously influenced by solvent effect, as it was proposed in a phenol/amine catalysis[70] and other HBD catalyzed ROPs summarized by Bibal recently.[23, 70]

Comparison between γ-resorcylic acid (RA) and salicylic acid (SA) and 3,5-dihydroxybenzoic acid in ROP of δ-valerolactone

To further elucidate the necessity of two HBDs in assistance of carboxylic in RA in enabling the catalytic activity in ROPs, salicylic acid (SA), a mono-phenol benzoic acid congener to RA, was chosen to promote ROP of VL (**Table 3**) as control. 3,5-dihydroxybenzoic acid, isomeric with RA, was chosen to compare the role of hydrogen bonds within the molecule by IR and ^{13}C NMR (**see Figure S4, S5**). We performed all the ROPs of VL by SA strictly under the same conditions as those by RA (***cf.* Table 1)**. The conversion of VL reached 17 % after 18 h at ratios of $[VL]_0/[BnOH]_0/[SA]$ = 30:1:1 (**Table 3, entry 1**). ROPs of VL with increasing the $[VL]_0/[BnOH]_0$ ratios from 50 to 150 (**Table 3, entries 2–5**) received low conversions (7–9 %) and high ratios of measured M_n to theoretical M_n (1.6 to 3.0 times discrepancies). These data showed *o*-hydroxyl benzoic acid (SA) mediated ROP of VL in solution at room temperature was not feasible, implied dual hydroxyls as IMHB in assistance to benzoic acid was essential.

Computational calculations on the bond lengths and partial charges in RA and SA influenced by H-bonding

To quantitatively demonstrate the formation and effects of IMHB in assistance of carboxylic acid in γ-resorcylic acid (RA) and salicylic acid (SA), density functional theory calculations were carried out at the B3LYP/6-31^{++}G level in Gaussian 09. RA and SA were optimized in geometries (**Figure 5**) and the relative bond lengths and energies were obtained. The bond length and partial charge pertaining to H-bonding in SA were assigned as r(O…H) = 1.7918 Å, and 0.498 (on **H** of carboxylic group); by comparison, H-bond lengths between one O—**H** and

Table 2. ROP of δ-valerolactone (VL) catalyzed by γ-resorcylic acid (RA) with benzyl alcohol (BnOH) as the initiator in different solvent after 18 h [a]

Entry	Solvent	Conv.[b] (%)	$M_{n,calcd}$ [c](g mol−1)	$M_{n,NMR}$ [b](g mol^{-1})	M_w/M_n [d]
1	dichloromethane	98	3040	3340	1.09
2	toluene	97	3020	3780	1.15
3	tetrahydrofuran	98	3040	3260	1.06
4	acetonitrile	76	2390	2690	1.06

[a]$[M]_0$ = 3.0 mol L^{-1}; room temperature. [b] Determined by ^{1}H NMR in $CDCl_3$. [c]Calculated from ($[M]_0/[BnOH]_0$) × conv. × (M_w of VL) + (M_w of BnOH). [d]Determined by SEC in THF using polystyrene standards.

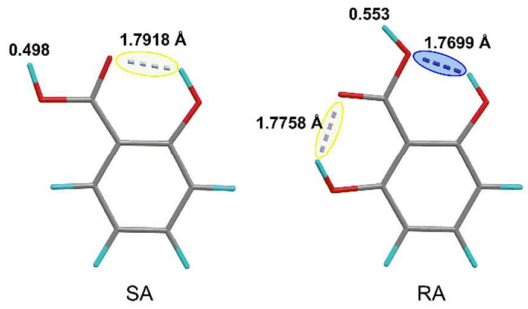


Figure 5. The comparison of hydrogen-bond lengths and partial charges on the polar hydrogen atoms of salicylic acid (SA) and γ-resorcylic acid (RA)

O (of C=O) was r(O…H) = 1.7758 Å, and another O—**H** to **O** (of carboxylic OH) was r(O…H) = 1.7699 Å, whereas the partial charge was 0.553 (on **H** of carboxylic group). The H-bond lengths in RA were short, and the H-bond angles were approaching 180°, which meant strong H-bonding formed in RA, partially due to the synergistic influence of the dual HBDs towards carboxylic.

As depicted in **Figure 6**, RA possessed shorter H-bond lengths and more polar H (of carboxylic OH) in comparison with those of SA, implied higher propensity of RA in releasing a proton (H^+), and would behave a stronger acid than ordinary benzoic acids. In fact, pK_a of RA was 1.30, meanwhile, the values of SA and benzoic acid were 2.98 and 4.20, respectively (**Scheme 4**, *vide infra*). RA sorted by pK_a just falls in the range of moderate acid; Although 2,4-dinitrobenzenesulfonic acid[71] and some Brønsted acids[72-74] presumably worked through bifunctional activations were successful in these ROPs. We proposed that the extraordinary activity of RA in ROPs might partially be attributed to the enhanced acidity by dual IMHB, whereas a full scenario of the role(s) of RA beyond sole cationic mechanism, and highly probable of bifunctional, deserved further investigations.

Proposed mechanism in ROP of δ-valerolactone by cationic monomer activation with γ-resorcylic acid

In order to evaluate the activating role of RA in the ROP of VL, NMR titration experiments were carried out (**Figure 6**). In the presence of RA, the chemical shifts of the carbonyl carbon of VL exhibited downfield shifts from 171.09 to 171.25 ppms with the increase of ratios of $[RA]/[M]_0$ from 1 to 2, which was attributed to the delocalization of electron densities by protonation on carbonyl. SA was taken as reference in the same NMR measurements at ratio of $[SA]/[M]_0$ = 2, smaller gap of a shift change (from 171.09 to 171.16 ppms) was observed. These data may explain why RA was active, but SA was not.

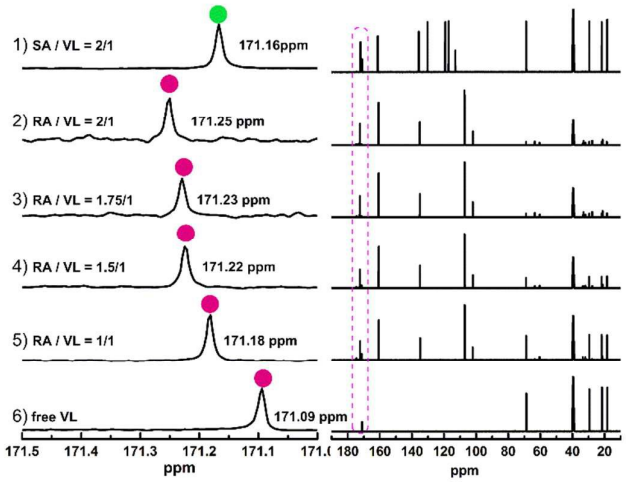


Figure 6. The chemical shifts of carbonyl carbon of VL in the ^{13}C NMR spectra (DMSO) observed in the presence of SA: 1) SA/VL = 2/1. The chemical shifts of carbonyl carbon of VL in the ^{13}C NMR spectra (DMSO) observed in the presence of RA: 2) RA/VL = 2/1, 3) RA/VL = 1.75/1, 4) RA/VL = 1.5/1, 5) RA/VL = 1/1

Herein, we put forward a plausible mechanism that dual intramolecular hydrogen-bonding assisted γ-resorcylic acid worked as a catalyst in the controlled/living ring-opening polymerization of δ-valerolactone via cationic monomer activating mechanism **(Scheme 3)**.

Hydroxybenzoic acids and phenol/benzoic acid pairs as congeners to γ-resorcylic acid in ROPs of δ-valerolactone

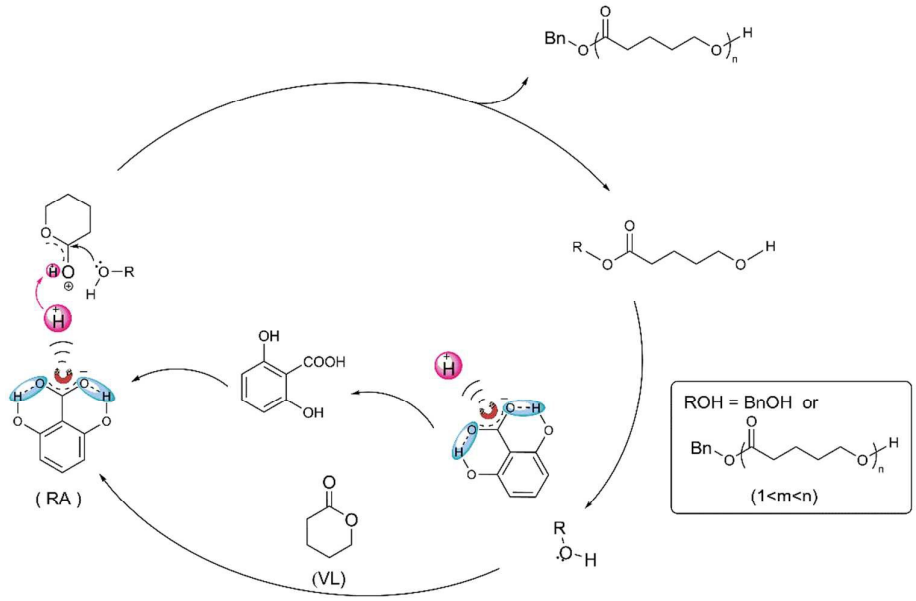
Further extension of possible combinations of phenol and benzoic acid functions by intra- and intermolecular H-bonding in catalysis was explored. Taken solution ROP of VL at conditions of $[VL]_0$ = 3.0 mol L^{-1}, $[VL]_0/[BnOH]_0/[Cat.]$ = 30:1:1, room temperature, and 18 h polymerization time as a benchmark experiment, seven catalysts (**Scheme 4, RA, SA, 1–5**) were tested. The conversions were measured by ^{1}H NMR and summarized in the supporting information (**Table S1**).

In brief, besides the optimal γ-resorcylic acid (**RA**) and a marginal inactive salicylic acid (**SA**), other catalysts showed essentially no promoting activity. From the melting points of the compounds (**Scheme 4, RA, SA and 1-3**), we may predict hydroxyl benzoic acids of low melting points (**RA** and **SA**) meant intramolecular H-bonding predominant, whereas hydroxyl benzoic acids of high melting points (**1–3**) suggested intermolecular H-bonding prevailing.

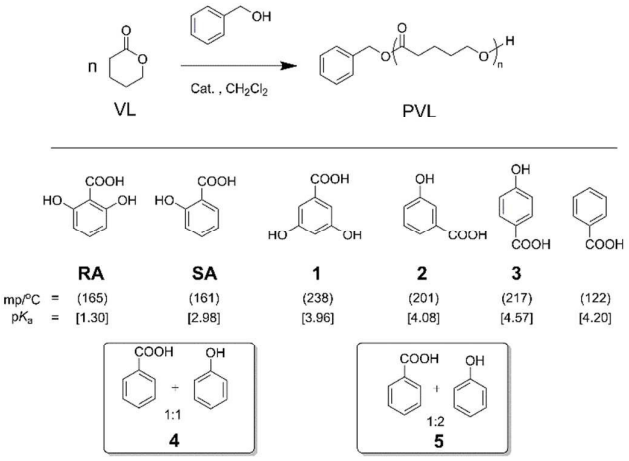
Table 3. ROP of δ-valerolactone (VL) catalyzed by salicylic acid (SA) with benzyl alcohol (BnOH) as the initiator[a].

Entry	M	[M]/[I]	Time (h)	Conv.[b](%)	$M_{n,calcd}$[c] (g mol^{-1})	$M_{n,NMR}$[b] (g mol^{-1})	M_w/M_n[d]
1	VL	30	18	17	630	1510	NA
2	VL	50	18	9	560	1540	NA
3	VL	75	22	7	660	1990	NA
4	VL	100	24	7	850	2040	NA
5	VL	150	36	9	1180	1920	NA

[a] $[M]_0$ = 3.0 mol L^{-1}; room temperature. [b] Determined by ^{1}H NMR in $CDCl_3$. [c] Calculated from ($[M]_0/[BnOH]_0$) ×conv. ×(M_w of VL) + (M_w of BnOH). [d] Not available, bimodal traces; determined by SEC in THF using polystyrene standards.



Scheme 3. Plausible activated monomer mechanism for RA-catalyzed ROP of VL using BnOH as the initiator



Scheme 4. ROP of δ-valerolactone (VL) catalyzed by various carboxylic acid catalysts (RA, SA and 1-5) with benzyl alcohol (BnOH) as the initiator. The numbers in parentheses represent relative melting point. The numbers in square brackets represent each p*K*a

Combinations of a benzoic acid and a phenol (mixtures **4** and **5**) as promoters showed no appreciable polymerization. These indicated that intermolecular H-bonding between a hydroxyl and a carboxylic was weak in solution; assistance of benzoic acid by phenolic hydroxyl was not up to an appreciable level as probed by ROP. The above experiments corroborated the assumption of dual IMHB enabled carboxylic acid active in the polymerizations.

Synthesis of poly-δ-valerolactones with clickable end-functions

For the purposes of evaluating the scope of RA-catalyzed polymerizations with controlled/living characteristics, we exploited ROPs of VL with propargyl alcohol, 5-hexen-1-ol, and N-(2-hydroxyethyl) maleimide as clickable[75, 76] initiators for providing end-functions (**Table 4**), which were confirmed by ^{1}H NMR spectra and MALDI-ToF MS measurements (**see Figure S6-S11**). The obtained polymers with functional end-groups were of potential modifications by azide–alkyne, thiol–ene, and Diels-Alder reactions. All the function-ended PVLs were

Table 4. Syntheses of end-functionalized polyesters by the RA-catalyzed ROP of VL using functional initiators in CH_2Cl_2 [a]

Entry	Initiator	Conv. [b](%)	$M_{n,calcd}$ (g mol^{-1})	$M_{n,NMR}$ [b](g mol^{-1})	M_w/M_n [d]
1	propagryl alcohol	98	2990	2340	1.17
2	5-hexen-1-ol	97	3000	2970	1.13
3	N-(2-hydroxyethyl) maleimide	96	3020	2760	1.10

[a] $[M]_0$ = 3.0 mol L^{-1}; room temperature. [b] Determined by ^{1}H NMR in $CDCl_3$. [c] Calculated from ($[M]_0/[BnOH]_0$) × conv. × (M_w of VL) + (M_w of BnOH). [d] Determined by SEC in THF using polystyrene standards.

exactly initiated from the corresponding initiators, the values of the molecular weights ($M_{n,NMR}$) and their distributions (M_w/M_n) were precisely ranged with in ideal intervals, and the conversions were reasonable for further derivations. These data suggested the RA catalyzed ROPs were practical in PVL preparations.

Conclusions

A conceptually new protocol of intramolecular hydrogen-bonding assisted Brønsted acid (IMHB–BA) catalysis in ring-opening polymerization was proposed. γ-Resorcylic acid (RA) as a model weak to moderate Brønsted acid demonstrated exceptional activity in ROPs of δ-valerolactone and ε-caprolactone in solutions at room temperature. This was the first example of Brønsted acid of weak to moderate strength workable in ROPs of lactones VL and CL. Controlled/living characteristics of RA catalyzed ROPs of lactones were certified by NMR measurements, chain extension polymerizations, and MALDI-ToF MS analysis. Homopolymers of VL and CL, and clickable end-functionalized PVLs were prepared; diblock copolymers of PVL-*b*-PCL by one-pot sequential feeding of VL and CL was successful; these results showed that RA catalyzed ROPs were general and practical. The extraordinary performances of RA were attributed to a dual IMHB by two OH in assistance of the carboxylic, in which two six-membered rings fused by the dual intramolecular H-bonding. The roles of the dual IMHB amongst two hydroxyls and one carboxylic, we named it as "three is company", were supported both by ^{13}C NMR titration, IR spectrum and by computational calculations. The dihydroxybenzoic acid RA catalysis in ROPs exemplified a spectacular control in molecular weights approaching Poisson distributions (Đ = 1.03). The IMHB–BA model suggested its resistance against solvent effect, showed high efficiency in nonpolar, polar, and hydrogen-bonding acceptor solvents. An extension of the IMHB assistance in organocatalysis of ROPs of diversity of monomers may lead rewarding area of mild and widely tolerance polymer preparations. In depth probe into the interactions amongst the IMHB, monomer, and the propagating chain is one of our future works.

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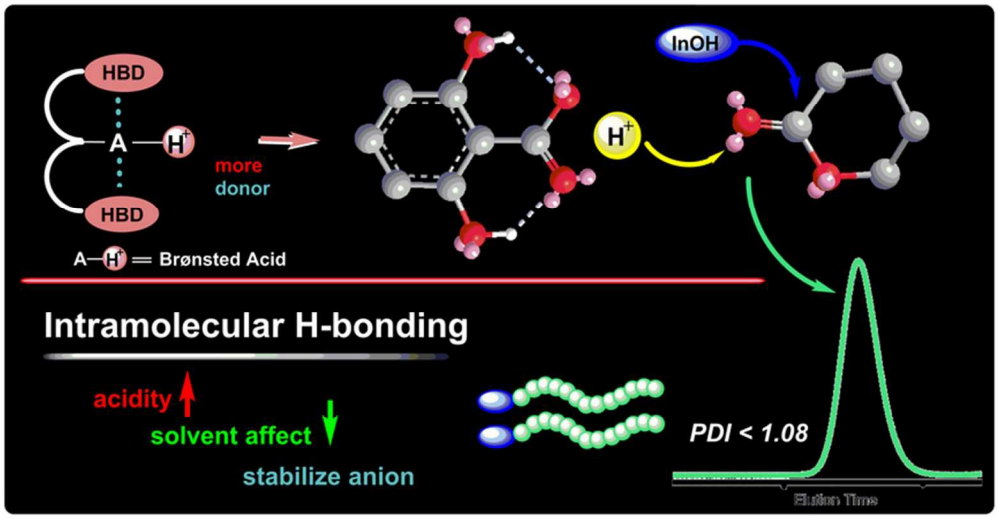

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