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Author(s)	Merlani, Maia; Koyama, Yasuhito; Sato, Hiroyasu; Geng, Li; Barbakadze, Vakhtang; Chankvetadze, Bezhan; Nakano, Tamaki
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Ring-opening Polymerization of a 2,3-Disubstituted Oxirane Leading to a Polyether Having a Carbonyl-Aromatic π-Stacked Structure†

Maia Merlani[a,b], Yasuhito Koyama[a], Hiroyasu Sato[c], Li Geng[a], Vakhtang Barbakadze[b], Bezhan Chankvetadze[d], Tamaki Nakano[*a]

2-Methoxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane was synthesized and polymerized using cationic initiator to afford a polymer having a rather stiff, stretched conformation. Side-chain methoxycarbonyl group and 3,4-dimethoxyphenyl group of neighboring monomeric units may form a hetero π-stacked structure between side-chain carbonyl and aromatic groups which leads to intramolecular charge transfer (ICT) interactions. 2-Ethoxycarbonyl-3-phenyloxirane failed in polymerization, leading only to small molecules including cyclic compounds.

Polyethers are an important class of polymers that find numerous applications. The most representative among polyethers may be poly(ethylene glycol) (PEG) made by ring-opening polymerization of oxirane (ethylene oxide),[1] and a variety of PEG derivatives are synthesized from mono-substituted oxiranes. In a sharp contrast, well-surveyed 2,3-disubstituted oxiranes are limited mainly to 2,3-dimethyloxirane,[2a,f,h] 2,3-bis(chloromethyl)oxirane,[2b,h] and 1,2-epoxycyclohexane,[2c-e,g,i,j-l] and polymerization of bulkier 2,3-disubstituted monomers has never been reported. This may be based on lower reactivity of such a monomer due to steric hindrance.

In this work, 2-methoxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane (MCDMPO) as an unsymmetrically 2,3-disubstituted oxirane monomer was synthesized and polymerized using a cationic initiator (Chart 1A). The design of MCDMPO is based on poly[2-hydroxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane] (poly[3-(3,4-dihydroxyphenyl)glyceric acid]) which is proposed to be an important ingredient contained in folk medicines widely used

in southern European countries.[3,4] MCDMPO is much bulkier than the aforementioned 2,3-disubstituted oxiranes, and hence its polymerization is a challenge. In addition, the obtained poly(MCDMPO) was found to have a stiff conformation leading to intramolecular charge-transfer (ICT) interactions.

In a sharp contrast to MDCMPO, 2-ethoxycarbonyl-3-phenyloxirane (ECPO) did not afford a polymer as major product but small molecules including diethyl 3,6-diphenyl-1,4-dioxane-2,5-dicarboxylate (I) and ethyl 2-benzyl-4-hydroxy-5-oxo-3-phenyl-2,5-dihydrofuran-2-carboxylate (II).

MCDMPO monomer was obtained from veratraldehyde (3,4-dimethoxybenzaldehyde, methyl vanillin) and methyl chloroacetate.[5] Although two diastereomers, the *anti* and *syn* isomers, are possible, the anti isomer was obtained in a pure form by recrystallization. The stereochemical assignment is based on the ^{1}H NMR analysis where the product showed only two doublet signals with a scalar coupling constant of 1.4 Hz for the two methine protons attached to the epoxide group (Fig. S5A in ESI).[6] ECPO was commercially available and was a mixture of the *anti* and *syn* isomers in the ratio of 86/14.
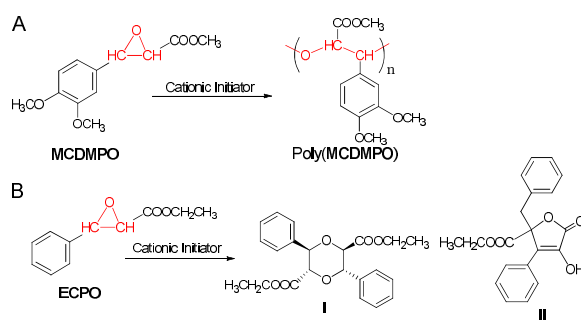
Chart 1 Cationic polymerization of MCDMPO (A) and ECPO (B).

MCDMPO was polymerized using $BF_3 \cdot OEt_2$ in CH_2Cl_2 under various conditions (Table 1). Under all conditions examined in this study, the monomer was almost completely consumed to afford a soluble polymer. The obtained polymers were isolated by reprecipitation in hexane. The chemical structure of the polymer indicated in Chart 1A is supported by ^{1}H and ^{13}C NMR (Fig. 1A and Fig. S5C in ESI) and MALDI-TOF mass (Fig. 1B) spectra. The

[a]*Catalysis Research Center (CRC) and Graduate School of Chemical Sciences and Engineering, Hokkaido University, N 21, W 10, Kita-ku, Sapporo 001-0021, Japan. Email:tamaki.nakano@cat.hokudai.ac.jp; Fax: +81-11-7069156; Tel: +81-11-7069155*

[b]*Kutateladze Institute of Pharmacochemistry, Tbilisi State Medical University, 36 str. P. Sarajishvili, 0159 Tbilisi, Georgia*

[c]*Rigaku Corporation 4-14-4, Sendagaya, Shibuya-Ku, Tokyo 151-0051, Japan*

[d]*Department of Physical and Analytical Chemistry, School of Exact and Natural Sciences, Tbilisi State University, Chavchavadze Ave 1, 0179 Tbilisi, Georgia*

mass spectrum indicated well-resolved signals spaced with mass numbers which are close to the unit molar mass (238.07); the observed mass numbers roughly correspond to molar masses of a polymer structure having an –OH group at a terminal (Fig. 1B, inset structure). The structure is reasonable for cationic polymerization where H_2O terminates a chain.

Table 1. Polymerization of MCDMPO with $BF_3 \cdot OEt_2$ in CH_2Cl_2 for 5 h[a,b]

| Run	T /°C	M/I	Y^c /%	M_n^d x10⁻³	M_w/M_n^e	α^f	K^f
1	23	20	83	3.8	1.18	0.90	3.2×10^{-5}
2	0	20	88	5.7	1.21	0.79	5.8×10^{-5}
3	−20	20	68	3.5	1.16	1.1	6.8×10^{-6}
4	−40	20	72	2.9	1.18	1.1	8.3×10^{-6}
5	0	10	93	4.5	1.76	0.44	1.7×10^{-3}
6	0	50	93	6.1	1.55	0.59	4.7×10^{-4}
7	0	100	95	8.7	2.48	0.82	7.2×10^{-5}
8	0	200	96	12.8	1.79	0.66	1.5×10^{-4}

[a]Monomer 200 mg, [monomer]₀ 0.84 M (runs 1-3, 5-8) or 0.60 M (run 4). [b]Monomer conversion ratio >99% as determined by ¹H NMR spectra of the crude mixture. [c]Yield of hexane-insoluble part. [d]Estimated by SEC with a right-angle laser light scattering and a viscometric detectors. [e]Estimated by SEC using standard polystyrenes. [f]Mark-Houwink-Sakurada coefficients.
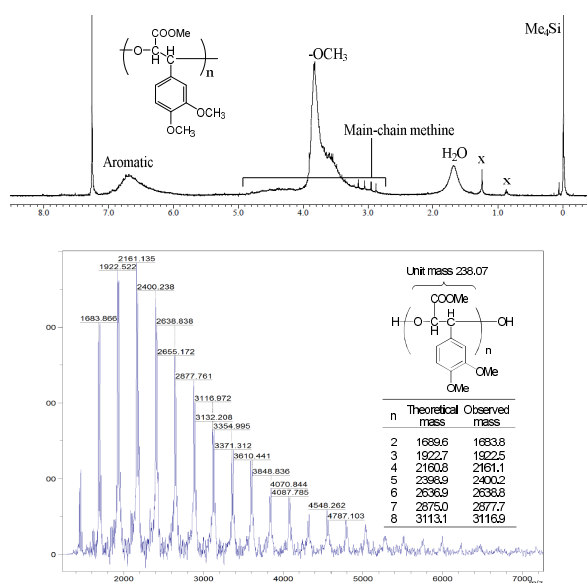
Fig. 1 400-MHz ¹H NMR spectrum of poly(MCDMPO) (run 7 in Table 1) (CDCl₃, at 23°C) (top) and MALDI−TOF mass spectrum of the polymer taken using α-cyano-4-hydroxycinnamic acid along with a chemical structure deduced from the spectrum and tabulated theoretical and observed mass numbers corresponding to the structure (bottom). X in the NMR spectrum denotes impurities.

Although Friedel-Crafts alkylation to the side-chain benzene ring by the growing cationic species could take place leading to a branched structure, the intensity ratio of the aromatic proton signals to the other signals in the ¹H NMR spectrum (ca. 3 to 11) is

consistent with the linear polymer structure shown in Chart 1A having three aromatic protons per residue. The extent of branch generation seems to be too low to be detected by ¹H NMR while possibility of branch cannot be completely ruled out.
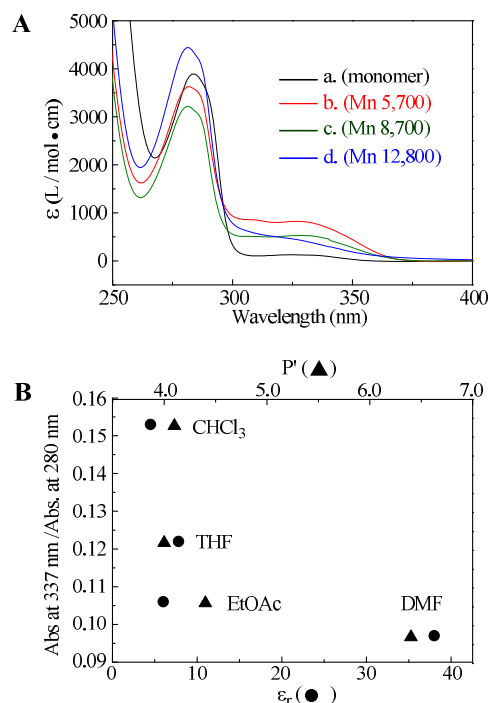
Fig. 2 UV spectra of MCDMPO monomer (a) and poly(MCDMPO)s of Mn 5,700 (b), 8,700 (c), and 12,800 (d) (A) and a plot of ratio of absorbance at 330 nm (ICT) to that at 280 nm (π−π*) of the polymer of Mn 12,800 against dielectric constant (ε_r) and Rohrschneider polarity parameter (P') of the solvent used for measurements (B). The spectra in A were taken in CHCl₃ at 1.7 x 10⁻⁴ M (a), 2.4 x 10⁻⁴ M (b), 2.4 x 10⁻⁴ M (c), and 2.0 x 10⁻⁴ M (d) at 23°C in a 1-mm quartz cell, and the data points in B were obtained from CHCl₃ (ε 4.5; P' 4.1), EtOAc (ε 6; P' 4.4), THF (ε 7.8; P' 4.0), and DMF (ε 38; P' 6.4) solutions at 1.0 x 10⁻⁵ M at 23°C.

M_n of the polymer ranged from 2,900 to 12,800 as determined by size-exclusion chromatography (SEC) with right-angle laser light scattering detection. From the results of entries 1 through 4 in Table 1, temperature seems not to have a significant effect on M_n of the products in the range of 23°C through −40°C. M_n was moderately controllable by changing [M]/[I] at 0°C (entries 2, 5−8 in Table 1).

Thermal analyses of the polymers indicated that the onset temperature of decomposition (T_d) and glass transition temperature (T_g) were 293.3°C and 88.3°C, respectively, for the polymer of M_n 8700 (run 7 in Table 1) (Figs. S11 and S12 in ESI).

Mark-Houwink-Sakurada coefficients (α) of the polymers were in the range of 0.44–1.11,[7] suggesting that conformation of the polymers is not completely flexible and may be rather stiff. For comparison, two typical polymers are raised here, *i.e.*, poly(hexyl

isocyanate)[8a-c] having a stiff, helical conformation and poly(oxy(methylsilylene))[8d] having a very flexible conformation; the former and the latter exhibit α value ranges of 0.77–1.10 and 0.21–0.28, respectively.[8,9] Although accurate discussions on conformation based only on the alpha values may be difficult due to the wide range of the alpha values and also due to rather low molar masses of the polymers, the photophysical properties and the molecular simulation results discussed hereafter are consistent of the proposed rather stiff conformation which is not very flexible.

Conformational and electronic characteristics were found also by ^{1}H NMR and absorbance spectra. ^{1}H NMR spectrum of poly(MCDMPO) indicated a broad aromatic signal in the range of 5.8 through 6.9 ppm which is up-field shifted with respect to the aromatic proton signals of the monomer (6.66-6.92 ppm) (Fig S5A in ESI). Further, the methoxy proton signals were also up-field shifted (polymer 3-3.9 ppm; monomer 3.82-3.88 ppm) (Fig S5A in ESI). The up-field shifts due to anisotropic magnetic effects of functional groups in ^{1}H NMR spectra are typical characteristics of stacked aromatic systems.[11] However, as discussed later, chain models indicate that distances between phenyl groups are too long to form a stack, and stacking may take place between carbonyl and 3,4-dimethoxylphenyl groups.

This assumption is supported by the broad absorbance band in the range of 300–370 nm in the UV spectra of the three polymers having different molar masses (Fig. 2A) which is absent in the monomer spectrum. This band is proposed to arise from ICT interactions between carbonyl and 3,4-dimethoxyphenyl groups.[10] Non-covalent ICT interactions have also been reported on vinyl copolymers bearing donor and acceptor side-chain chromophores.[10c,d] Intensity of this band is rather low and ICT interactions hence may be weak. The fact that the three polymers indicated slightly different UV spectral shapes might mean that their stereo structures are not completely uniform.

Solvent polarity has been pointed out to affect ICT.[10e] Solvent effects on UV spectrum of the polymer of Mn 12,800 were investigated using CHCl$_3$, tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF) and acetone. A rough tendency was found that the ratio of absorbance at 337 nm (ICT) to that at 280 nm (π–π*) which may be correlated to population of ICT-causing stacked species decreased with an increase in dielectric constant (ε$_r$) and Rohrschneider polarity parameter (P')[12] of the solvent of measurement at a constant concentration of [MCDMPO residue] = 1.0 x 10^{-5} M (Fig. 2B). This may mean that population of well-interacting π-stacked carbonyl-3,4-dimethoxylphenyl combination is lower in a more polar solvent where polar interactions between solvent molecules and the chromophores destabilize stacking.

Scheme 1. Head-to-tail growth with inversion (left) and retention right) of C(2) configuration in MCDMPO polymerization.
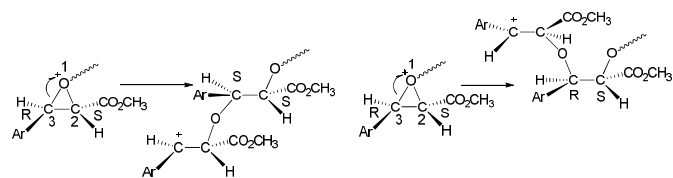
Polymer conformation in connection with intrachain chromophore interactions was assessed by molecular dynamics (MD) simulations 20-mer models. Although main-chain configuration of the polymer has not yet been determined, head-to-tail structure is reasonably assumed because the O-C(3) bond would more readily break than the O-C(2) bond on ring-opening because the resulting cation can be stabilized by 3,4-dimethoxyphenyl group (Scheme 1). Retention of configuration at C(3) leads to an (R,S)-unit while inversion at C(3) an (S,S)-unit, and preferred stereochemistry is not clear, leading to many possibility of structures. Thus, as representative head-to-tail type chain structures, five 20-mer models with different main-chain configurations were examined (Fig. S13 in ESI).
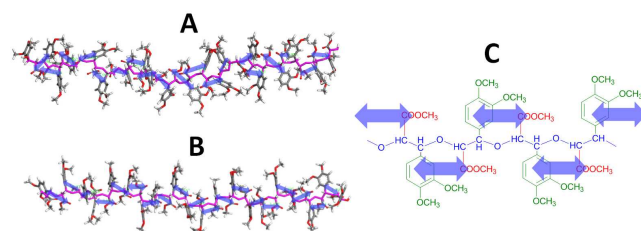
Fig. 3 Structures obtained through MD simulations for 5 nsec for at 297 K (S,S)-20-mer (A), (S,S)/(R,R)-20-mer (B), and a schematic drawing of a chain (C). In A and B, white, gray, and red correspond to H, C, and O, respectively, and pink the main chain. Blue arrows indicate carbonyl-aromatic combinations that may contribute to ICT interactions.

During simulations for 5 nsec at 297 K, (S,S)-20-mer and (S,S)/(R,R)-20-mer remained as stretched chains (Fig. 3A,B) which is consistent with the α values while the other chains largely deviated from a stretched conformation (Fig. S13 in ESI). For all models, the distance between neighboring dimethoxyphenyl groups seems too long to form a stack. On the other hand, as for (S,S)-20-mer and (S,S)/(R,R)-20-mer, carbonyl and aromatic groups belonging to adjacent units are located close enough to interact with each other through local bond rotations. The averaged distance between such carbonyl and aromatic groups as defined as a distance between the carbonyl carbon and the 1-position carbon of phenyl group was 3.5 Å for (S,S)-20-mer and 3.7 Å for (S,S)/(R,R)-20-mer which are rather close to the stacking distance in DNAs (3.4 Å).[13] These results support that the proposed ICT interactions.

It should be noted here that carbonyl-aromatic interactions have been recognized for proteins.[14]
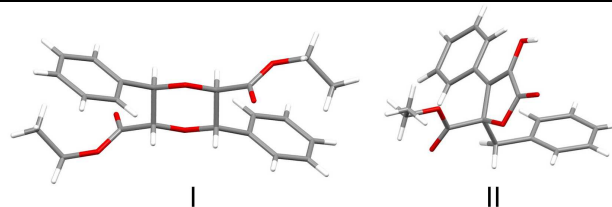
Fig. 4. Crystal structures of 3,6-diphenyl-1,4-dioxane-2,5-dicarboxylate and ethyl 2-benzyl-4-hydroxy-5-oxo-3-phenyl-2,5-dihydrofuran-2-carboxylate (I and II, respectively, in Chart1).

In reference with the polymerization of MCDMPO, polymerization of ECPO, a similar monomer, was attempted using $BF_3 \cdot OEt_2$ and Tf_2O as cationic initiators in CH_2Cl_2 and toluene. However, polymer was not obtained as a major component with either initiator. The major products from the reactions using $BF_3 \cdot OEt_2$ in toluene at 110^oC and using Tf_2O were diethyl 3,6-diphenyl-1,4-dioxane-2,5-dicarboxylate and ethyl 2-benzyl-4-hydroxy-5-oxo-3-phenyl-2,5-dihydrofuran-2-carboxylate (I and II in Chart1), respectively, whose structures were disclosed by X-ray crystal structure analysis (Fig. 4). These results indicate that polymerizability of MCDMPO arises from stabilization of intermediate cation by the dimethoxyphenyl group. The phenyl group of ECPO having no electron-donating the menthoxy groups appear not be sufficient for cation stabilization. The structure of I may be recognized as a head-to-tail cyclic dimer, which may support the proposed head-to-tail structure of poly(MCDMPO).

In conclusion, MCDMPO leads to a polymer having a rather stiff conformation having a novel π-stacked structure between aromatic and carbonyl groups of neighbouring monomeric units, leading to ICT interactions. Although regulated π-stacked structures of a polymer have been prepared for accumulated aromatic groups in the side- and main-chain,[11,15] such a "hetero □-stacked conformation" of polymer chain consisting of different types of □-electron systems is unprecedented to the best of our knowledge. We can hence conclude that a properly designed, bulky, 2,3-disubstituted oxirane can lead to a polymer having a specific conformation that can result in intriguing properties.

Acknowledgements

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TOC graphic
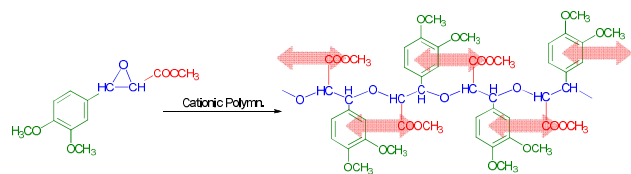
Ring-opening polymerization of a 2,3-disubstituted oxirane afforded to a polyether exhibiting intramolecular charge-transfer (ICT) interactions due to a carbonyl-aromatic π-stacked conformation.