Amino Acid-Functionalized Ethyl Cellulose: Synthesis, Characterization, and Gas Permeation Properties

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ABSTRACT: Amino acid esters of ethyl cellulose [R′ = H (**1**), CH_3 (**2**), $CH_2CH(CH_3)_2$ (**3**), CH_2CONH_2 (**4**), $CH_2OCH_2C_6H_5$ (**5**, **5′**), $CH_2CH_2CH_2CH_2NHOCOC(CH_3)_3$ (**6**)] were synthesized in moderate to quantitative yields (30–99%) by the reaction of *t*-butoxycarbonyl (*t*-Boc)-protected amino acids or an activated ester derivative with hydroxy groups of ethyl cellulose [EC; degree of substitution (DS_{Et}), 2.69]. The amino acid functionalities displaying varied chemical nature, shape, and bulk were used, and bulk of the substituent on the α-carbon of amino acids was elucidated to be of vital significance for the observed degree of incorporation (DS_{Est}). ^1H NMR spectra were used to determine the degree of incorporation of amino acid moiety (DS_{Est}), and almost complete substitution of the hydroxy protons was revealed in **1**, **2**, and **5′**. The onset temperatures of weight loss of **1**–**6** were 198–218 °C, indicating fair thermal stability. The glass transition temperatures of the derivatized polymers were 30–40 °C lower than that of EC (T_g 131 °C; cf. T_g of **1**–**6**, 93.5–103 °C). Free-standing membranes of EC and its amino acid esters (**1**, **2**, **5**, **5′**, and **6**) were fabricated, and enhanced permselectivity for CO_2/N_2 and CO_2/CH_4 gas pairs was discerned, when compared with EC. © 2010 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 48: 3986–3993, 2010

KEYWORDS: amino acid; esterification; ethyl cellulose; gas permeation; glass transition

INTRODUCTION Cellulose is an inexhaustible natural polymeric material with a polyfunctional macromolecular structure and an environmentally benign nature, but its supramolecular architecture confers it with lack of solubility thus making its derivatization quite cumbersome. However, ethyl cellulose (EC), one of the commercially important cellulose ethers, is an odorless, thermoplastic, nonionic, and nontoxic polymer displaying excellent solubility in a wide range of common organic solvents.[1–4] Owing to its ability to serve as an emulsifier and as a coating, binding, and film-forming agent, EC finds a multitude of industrial applications in food, industrial coatings, and textile printing. EC has also been extensively used in pharmaceutical formulations as a tablet binder, film-coating material, and thickening agent, and so forth, and particularly as a hydrophobic matrix in controlled-release dosage forms because it is a water-insoluble, nontoxic, nonallergenic, and nonirritant material.[5–7] Moreover, it is worth mentioning that EC is a commercially available low-cost cellulosic characterized by its adequacy to form chemically resistant and mechanically tough free-standing membranes, exhibiting moderate gas permeation/pervaporation capability.[8–17] EC, being widely used as a pharmaceutical excipient and extensively studied as a membrane-forming material, possesses free hydroxy groups serving as the sites of chemical derivatization and offers the possibility to bring about the modification of various properties. The synthesis of EC derivatives with polar side chains might be expected to increase the CO_2 permselectivity of the resulting polymeric materials thus rendering them potentially more suitable for CO_2 separation membranes.

Amino acids are basic building blocks of nature capable of accomplishing a variety of exquisite functions spanning the horizons of natural to synthetic materials, serving the multifarious domains of life including food, drugs, and fibers, and playing a prominent role in the world of synthetic architectures as chiral sources for organic synthesis and optical resolution materials. In the past few decades, synthesis of amino acid- and peptide-containing polymers has attracted considerable attention because a high degree of amino acid functionality and chirality can confer the polymers with the

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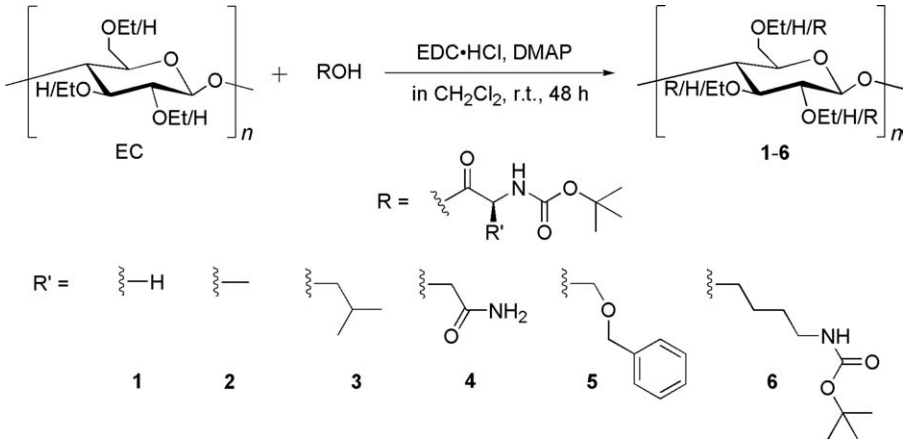


SCHEME 1 Esterification of EC using a condensation agent.

unique features of enhanced solubility, regulated higher order structures/helix formation, stimuli-responsiveness, and liquid crystalline arrangement.[18–27] Furthermore, amino acids and peptides are widely used in the synthesis of biocompatible architectures, finding quite promising applications as controlled drug delivery systems, cell-adhesive structures, polyelectrolytes, chiral recognition materials, and medicines.[28–37] However, there has been only one comprehensive report regarding the gas permeation characteristics of synthetic polypeptide [poly(α-amino acid)] membranes, elucidating a high-permeation selectivity particularly for CO_2.[38]

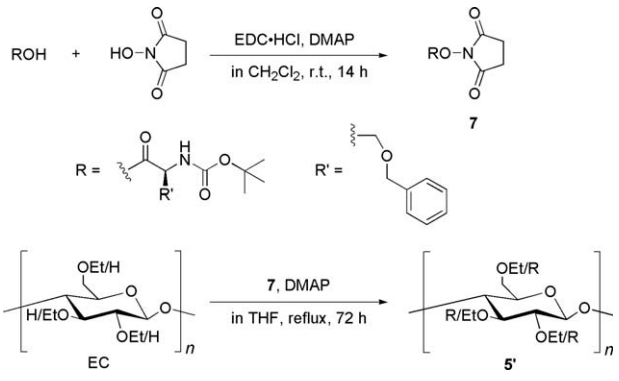
Although the amino acid-containing polymers have engrossed substantial prominence as a new class of bioactive polymeric materials,[18–37] only a few significant research endeavors concerning the amino acid functionalization of cellulose derivatives have been reported so far.[39] The hydroxy anchors of EC and the carboxy termini of amino acids provide an ample opportunity of bringing about a successful conjunction of the two biocompatible families of materials. Our previous efforts to effect the derivatization of organosoluble cellulosic polymers with a variety of substituents are quite evident of the fact that the tailoring of pendants on the cellulosic backbone results in a significant alteration of solubility, thermal, charge/discharge, and gas permeation characteristics as desired for specific applications.[39–45] Hence, amino acid esterification of EC is anticipated to lead to the enhanced CO_2 separation performance, making these materials interesting candidates for gas separation membranes.

The present contribution describes the synthesis and characterization of amino acid-functionalized EC derivatives (**1–6**) (Schemes 1 and 2). A clear dependence of degree of esterification (DS_{Est}) on the bulk of the substituent on the α-carbon of amino acids has been revealed. The solubility characteristics and thermal properties of the derivatized polymers were elucidated. Moreover, free-standing membranes of starting as well as resulting polymers (EC and **1–6**) were fabricated and their gas permeation parameters were determined.

EXPERIMENTAL

Measurements

^{1}H NMR spectra were recorded on a JEOL EX-400 spectrometer, and the residual proton signal of the deuterated solvent was used as internal standard ($CHCl_3$: δ 7.24 ppm). The number- and weight-average molecular weights (M_n and M_w, respectively) and polydispersity indices (M_w/M_n) of polymers were estimated by GPC at 40 °C with a Jasco PU-980/RI-930 chromatograph (eluent THF, column KF-805 (Shodex) × 3, molecular weight range up to 4×10^6, flow rate 1 mL/min). The elution times were converted into molecular weights using a calibration curve based on polystyrene standards in combination with the information obtained from the refractive index detector. Thermogravimetric analyses (TGA) were conducted in air with a Shimadzu TGA-50 thermal analyzer by heating the samples (5–7 mg) from 100–700 °C at a scanning rate of 10 °C min^{-1}. Differential scanning calorimetric (DSC) analyses were performed using a Seiko DSC6200/EXSTAR6000 apparatus, and measurements were carried out by making use of 3–5 mg samples, under a nitrogen atmosphere, after calibration with an indium standard. The samples were first heated from ambient temperature (25 °C) to 200 °C at a scanning rate of 20 °C min^{-1} (first heating scan) and then immediately quenched to −50 °C at a rate of about 80 °C min^{-1}. The second heating scans were run from −50 to 200 °C at a scanning rate of 20 °C min^{-1} to record stable thermograms. The glass transition temperature (T_g) data were obtained from the second run and correspond to the midpoint of discontinuity in the heat flow.



SCHEME 2 Synthesis of an activated ester of amino acid and its reaction with EC.

Materials

EC (ethoxy content, 49 wt %; degree of substitution by ethyl group (DS_{Et}) per anhydroglucose unit (AGU), 2.69; Aldrich), 4-(dimethylamino)pyridine (DMAP; Wako), and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl; Eiweiss Chemical) were commercially obtained and used as received. *N*-α-*t*-Butoxycarbonyl (*t*-Boc)-L-glycine, *N*-α-*t*-Boc-L-alanine, *N*-α-*t*-Boc-L-leucine, *N*-α-*t*-Boc-L-asparagine, *N*-α-*t*-Boc-*O*-benzyl-L-serine, and *N*-α-,*N*-ε-di-*t*-Boc-L-lysine were purchased from Watanabe Chemical Ind. (Japan). Dichloromethane (CH_2Cl_2), used as the reaction solvent, was purchased from Wako (Japan) and used without further purification.

Synthesis

Synthetic procedures and spectral data of amino acid esters of EC (**1–6** and **5**′ in Schemes 1 and 2, respectively) are described below.

N-α-t-*Butoxycarbonyl-L-glycine Ester of EC (1) by Using EDC·HCl*

A 200-mL one-necked flask was equipped with a stopper and a magnetic stirring bar. EC (1.00 g, 4.21 mmol of AGUs) was added into the flask and dissolved in CH_2Cl_2 (30 mL) at room temperature. DMAP (0.0772 g, 0.632 mmol) was introduced, followed by the addition of *N*-α-*t*-Boc-L-glycine (1.11 g, 6.34 mmol) and EDC·HCl (1.21 g, 6.32 mmol). After stirring for 48 h at room temperature, the reaction mixture was added dropwise to an aqueous $NaHCO_3$ solution (1000 mL) to precipitate the product, which was filtered with a membrane filter, washed with water several times to ensure the complete removal of $NaHCO_3$, and dried under vacuum to constant weight to afford the desired compound as a white solid.

Yield 99%, ^{1}H NMR ($CDCl_3$, ppm): δ 5.66−2.88 (m), 1.58−1.33 (brs), 1.35−0.94 (brs).

N-α-t-*Butoxycarbonyl-L-alanine Ester of EC (2) by Using EDC·HCl*

This derivative was prepared by the same procedure as for **1** using *N*-α-*t*-Boc-L-alanine instead of *N*-α-*t*-Boc-L-glycine.

Yield 99%, ^{1}H NMR ($CDCl_3$, ppm): δ 5.40−2.72 (m), 1.58−1.49 (brs), 1.49−1.31 (brs), 1.24−0.78 (brs).

N-α-t-*Butoxycarbonyl-L-leucine Ester of EC (3) by Using EDC·HCl*

This derivative was prepared by the same procedure as for **1** using *N*-α-*t*-Boc-L-leucine instead of *N*-α-*t*-Boc-L-glycine.

Yield 99%, ^{1}H NMR ($CDCl_3$, ppm): δ 5.45−2.72 (m), 2.27−2.15 (brs), 1.50−1.37 (brs), 1.37−1.02 (brs).

N-α-t-*Butoxycarbonyl-L-asparagine Ester of EC (4) by Using EDC·HCl*

This derivative was prepared by the same procedure as for **1** using *N*-α-*t*-Boc-L-asparagine instead of *N*-α-*t*-Boc-L-glycine.

Yield 99%, ^{1}H NMR ($CDCl_3$, ppm): δ 5.32−2.72 (m), 2.52−1.80 (brs), 1.46−1.34 (brs), 1.34−0.60 (brs).

N-α-t-*Butoxycarbonyl-O-benzyl-L-serine Ester of EC (5) by Using EDC·HCl*

This derivative was prepared by the same procedure as for **1** using *N*-α-*t*-Boc-*O*-benzyl-L-serine instead of *N*-α-*t*-Boc-L-glycine. After washing with water, the reaction product was dissolved in CH_2Cl_2, isolated by precipitation into DMSO, filtered with a membrane filter, and dried under vacuum to constant weight to afford the desired compound as a white solid.

Yield 78%, ^{1}H NMR ($CDCl_3$, ppm): δ 7.42−7.17 (brs), 5.10−2.68 (m), 1.65−1.37 (brs), 1.37−0.72 (brs).

N-α-,N-ε-*di*-t-*Butoxycarbonyl-L-lysine Ester of EC (6) by Using EDC·HCl*

This derivative was prepared by the same procedure as for **1** using *N*-α-,*N*-ε-di-*t*-Boc-L-lysine instead of *N*-α-*t*-Boc-L-glycine.

Yield 30%, ^{1}H NMR ($CDCl_3$, ppm): δ 5.42−2.69 (m), 2.12−1.91 (brs), 1.68−1.31 (brs), 1.31−0.58 (brs).

Activated Ester of N-α-t-*Butoxycarbonyl-O-benzyl-L-serine (7)*

A 200-mL one-necked flask was equipped with a stopper and a magnetic stirring bar. *N*-Hydroxysuccinimide (0.288 g, 2.50 mmol), DMAP (0.0305 g, 0.250 mmol), *N*-α-*t*-Boc-*O*-benzyl-L-serine (0.739 g, 2.50 mmol) and EDC·HCl (0.479 g, 2.50 mmol) were added into the flask and dissolved in CH_2Cl_2 (20 mL). After stirring for 14 h at room temperature, the reaction mixture was washed with 0.5 M HCl, saturated aqueous $NaHCO_3$ solution, and saturated aqueous NaCl solution, successively. The obtained organic layer was dried over anhydrous $MgSO_4$, filtered through membrane filter, and then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography [eluent: hexane/ethyl acetate (4:1)] to afford **7** as a white solid.

Yield 81%, ^{1}H NMR ($CDCl_3$, ppm): δ 7.35−7.22 (m), 5.45−5.35 (d), 5.13−5.05 (brs), 4.85−4.78 (d), 4.65−4.58 (d), 4.58−4.50 (d), 4.00−3.88 (dd), 3.81−3.75 (dd), 2.91−2.72 (s), 1.55−1.30 (s).

N-α-t-*Butoxycarbonyl-O-benzyl-L-serine Ester of EC (5′) by Using Activated Ester (7)*

A 200-mL one-necked flask was equipped with a stopper and a magnetic stirring bar. EC (0.319 g, 1.34 mmol of AGUs) was added into the flask and dissolved in THF (20 mL) at room temperature. DMAP (0.0772 g, 0.632 mmol) was introduced, followed by the addition of **7** (0.792 g, 2.01 mmol), and stirring was continued for 72 h along with heating under reflux. The product was isolated by precipitation in aqueous $NaHCO_3$ solution (1000 mL), filtered with a membrane filter, washed with water several times to ensure the complete removal of $NaHCO_3$, and dried under vacuum to constant weight to afford the desired compound as a white solid.

Yield 50%, ^{1}H NMR ($CDCl_3$, ppm): δ 7.30−7.10 (brs), 5.66−2.88 (m), 1.58−1.33 (brs), 1.35−0.94 (brs).

Membrane Fabrication

Membranes (thickness ca. 40–80 μm) of EC and **1–6** were fabricated by casting their toluene solution (concentration ca. 0.50–1.0 wt %) onto a flat-bottomed Petri dish. The dish was covered with a glass vessel to retard the rate of solvent

TABLE 1 Esterification of Ethyl Cellulose with Amino Acids

Polymer	Yield (%)	DS_{Est}[a] (%)	M_n[b]	M_w/M_n[b]
EC	–	–	49,000	3.2
1	99	100	61,000	2.9
2	99	100	66,000	3.1
3	99	15	55,000	3.4
4	99	18	52,000	3.3
5	78	69	97,000	2.7
5′	50	100	105,000	2.3
6	30	80	102,000	2.3

[a] DS_{Est}, degree of esterification. Calculated from ^{1}H NMR measurement in $CDCl_3$.
[b] Estimated by GPC (THF, PSt).

evaporation (3–5 days). Membrane thickness was estimated by using a Mitutoyo micrometer.

Measurement of Gas Permeability Coefficients

The gas permeability coefficients (P) were measured with a Rikaseiki K-315-N gas permeability apparatus using a constant volume/variable-pressure system. All of the measurements were carried out at 25 °C and a feed pressure of 0.1 MPa (1 atm), while the downstream side of the membrane in the system was being evacuated. The P values were calculated from the slopes of the time-pressure curves in the steady state where Fick's law holds.[46]

RESULTS AND DISCUSSION

Amino Acid Esterification of Ethyl Cellulose

The amino acid esterification of EC was accomplished by coupling the hydroxy functionalities of EC with the carboxy termini of amino acids bearing *t*-Boc-protected amino moieties; *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC·HCl) was used as a condensation agent, 4-(dimethylamino)pyridine (DMAP) as a base, and CH_2Cl_2 as a solvent (Scheme 1). In another attempt, activated ester of amino acid (**7**) was synthesized, followed by its reaction with EC in the presence of DMAP in THF (Scheme 2). The results are summarized in Table 1. The DS_{Et} of EC was estimated to be 2.69, by calculating the integration ratio of methyl protons to the rest of the protons in the ^{1}H NMR spectrum of EC, indicating the presence of 0.31 hydroxy groups per AGU.[40,42,44,45] The ^{1}H NMR spectral data of amino acid esters of EC (**1**–**6**) were obtained to determine the degree of substitution by ester group, namely aminoalkanoyl substituent, (DS_{Est}) by making an estimation of the peak intensity ratios of the terminal methyl protons of ethyl group of EC and those of *t*-Boc moieties of the amino acid pendants. The DS_{Est} of amino acid esters of EC, synthesized by using a condensation agent, was discerned to be primarily affected by the bulk of the substituent on the α-carbon of the amino acid moieties, and the residual hydroxy protons of the starting cellulosic were quantitatively substituted only in the *t*-Boc-protected glycine- and alanine-derivatized polymers (**1** and **2**: DS_{Est}, 100%). On the other hand, in leucine- and asparagine-derived polymers (**3** and **4**), the presence of bulky isobutyl and amide groups was attended by quite low degree of esterification (**3**: DS_{Est}, 15%; **4**: DS_{Est}, 18%); nevertheless, serine- and lysine-functionalized (**5** and **6**) polymers displayed fairly high extent of amino acid incorporation (**5**: DS_{Est}, 69%; **6**: DS_{Est}, 80%) owing to the presence of relatively planar benzyl group and comparatively longer butylene spacer in **5** and **6**, respectively. The aminoalkanoylation of EC by using an activated ester of *N*-α-*t*-Boc-*O*-benzyl-L-serine (**7**) accomplished the complete esterification (**5**′: DS_{Est}, 100%).

The molecular weights of the starting (EC) as well as derivatized polymers (**1**–**6**) were estimated by gel permeation chromatography, and the data are listed in Table 1. The esterification of EC involving the substitution of small hydroxy protons with bulky organic moieties accompanied an increase in the molecular weight of the polymers; for example, the M_n of EC was observed to be 49 000, while those for **1**–**6** were 52,000–105,000, respectively. Moreover, the polydispersity indices (M_w/M_n) of the amino acid-functionalized polymers (**1**–**6**) were not quite different from those of EC; for instance, the M_w/M_n of EC and **1**–**6** were 3.2 and 2.3–3.4, respectively, thus ruling out the possibility of polymer chain cleavage under the mild reaction conditions used for esterification.

Solubility and Thermal Properties of the Polymers

The solubility characteristics of EC and its amino acid esters (**1**–**6**) are shown in Table 2. EC is soluble in polar protic solvents such as methanol, highly polar aprotic solvents like DMF, and partly soluble in moderately polar acetone. Upon the incorporation of aminoalkanoyl substituents, the solubility in methanol and DMF was retained, whereas **1**–**6** were completely or partly soluble in acetone, and this tendency can reasonably be attributed to the presence of polar carbamate (protected amino) and ester linkages. Despite the introduction of polar substituents, the solubility behavior of derivatized polymers (**1**–**6**) in THF, $CHCl_3$, and toluene was also the same as that of the starting polymer (EC) presumably by virtue of peripheral *t*-butyl groups. Thus, it can be inferred that the amino acid esterification of EC has led to an overall improvement in the organosolubility particularly in acetone.

The thermal stability of the polymers (EC and **1**–**6**) was examined by TGA in air (Table 3 and Fig. 1). The onset temperature of weight loss (T_0) of EC was 311 °C, whereas those for **1**–**6** were in the range of 198–218 °C. The TGA curves of all the amino acid esters (**1**–**6**) exhibited an almost identical pattern of three-step weight loss commencing at approximately 200, 300, and 370 °C, respectively. In contrast, a two-step weight loss was observed with the starting cellulosic. For **1**–**6**, the decomposition at first stage should be the cleavage of peripheral *t*-Boc groups because the *t*-butyl moiety is thermally labile to release isobutene above 180 °C.[47–49]

The T_g values of the polymers (EC, **1**, **2**, **5**, and **6**) were determined by DSC under nitrogen (Fig. 2). However, **5**′ exhibited no T_g up to 200 °C. The incorporation of *t*-Boc-protected amino acid pendants was observed to accompany a decrease in the T_g of polymers; for instance, those of EC and its amino acid esters were 131 and 93.5–103 °C, respectively

TABLE 2 Solubility[a] of EC and **1–6**

Polymer	DS_{Est} (%)	Hexane	Toluene	$CHCl_3$	THF	Acetone	Methanol	DMF
EC	–	–	+	+	+	±	+	+
1	100	–	+	+	+	+	+	+
2	100	–	+	+	+	+	+	+
3	15	–	+	+	+	±	+	+
4	18	–	+	+	+	±	+	+
5	69	–	+	+	+	+	+	+
5′	100	–	+	+	+	+	+	+
6	80	–	+	+	+	+	+	+

[a] Symbols: +, soluble; –, insoluble; ±, partly soluble.

(Table 3). The variation in the glass transition temperature of the polymeric materials is dramatically affected by the nature of side chains, and the increased polarity entails enhanced T_g values and vice versa. On the other hand, the bulk and shape of the substituents are also of vital significance, and the presence of spherical bulky substituents augments the chain flexibility and thus ensues the reduced T_g.[50] In our previous studies concerning the dendronization of EC, the presence of polar amide-containing dendritic wedges with bulky and spherical nonpolar periphery has been reported to lead to a considerable decrease in the T_g of the polymers.[42] Similarly, the present series of polymers (**1–6**) is characterized by the presence of polar amino and ester linkages along with fairly bulky and spherical nonpolar periphery, probably the latter being more dominant in the determination of T_g. Hence, the substitution of small hydroxy protons by bulkier aminoalkanoyl functionalities has resulted in the lowering of T_g in the present series of polymeric materials.

Gas Permeability of the Polymers

The permeability coefficients of membranes of EC, **1**, **2**, **5**, **5′**, and **6** to helium, hydrogen, nitrogen, oxygen, carbon dioxide, and methane, determined from the steady state transport of each pure gas at 25 °C, are listed in Table 4. The P values of the amino acid-functionalized polymers were lower than those of EC, and their magnitude seems to be determined by the shape, size, chemical nature, and mobility of the pendant groups.

This study reveals the effect of the incorporation of amino acid pendants on the gas permeation characteristics of EC. To date, there have been few reports concerning the amino acid functionalization of EC and outcomes of this successful conjunction as a membrane-forming material. In polymeric membranes, the decrement of gas permeability emanating from the introduction of polar substituents due to the reduced free volume inside the polymer matrix is a well-established concept.[42,51–57] As seen from Table 4, the substitution of small hydroxy protons of EC with relatively bulky and polar aminoalkanoyl substituents resulted in the decreased permeability coefficients for all the gases; for example, the P_{O_2} and P_{N_2} of EC are 25 and 7.8 barrers and those observed for its derivatized counterparts were 9.5–13 and 2.4–3.6 barrers, respectively. These trends in the gas

TABLE 3 Thermal Properties of EC and **1–6**

Polymer	DS_{Est} (%)	T_0[a] (°C)	T_g[b] (°C)
EC	–	311	131
1	100	216	97.4
2	100	200	103
3	15	198	–[c]
4	18	215	–[c]
5	69	211	101
5′	100	212	–[d]
6	80	218	93.5

[a] Onset temperature of weight loss. Observed from TGA measurement in air (heating rate 10 °C min^{-1}).
[b] Glass transition temperature. Determined by DSC analysis under N_2 (second scan, heating rate 20 °C min^{-1}).
[c] Not measured.
[d] No T_g was observed up to 200 °C.

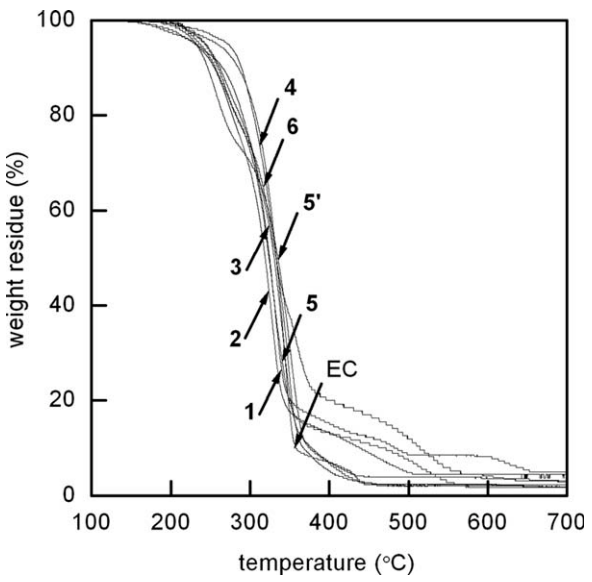


FIGURE 1 TGA curves of EC and **1–6** (in air, heating rate 10 °C min^{-1}).

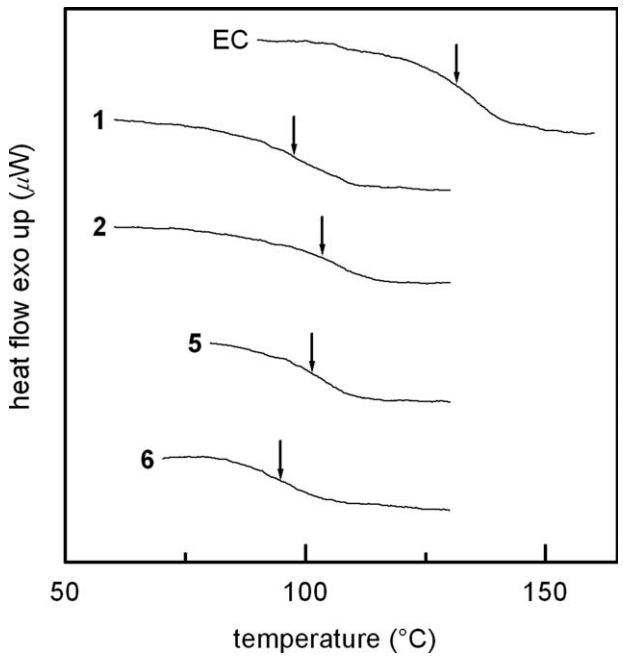


FIGURE 2 DSC thermograms of EC, **1**, **2**, **5**, and **6** (under N_2, heating rate 20 °C min^{-1}).

permeability of amino acid-functionalized polymers can reasonably be ascribed to the presence of polar (amino and ester) groups resulting in a denser chain packing, leading to the reduced free volume inside the polymer matrix, and in turn lower gas permeability. The gas permeability did not vary significantly with the change in the substituent on α-carbon of the amino acid functionalities as they possess great similarity in composition and shape. However, subtle variations in the gas permeability emanating from the slight structural modification did not go unnoticed; for instance, the carbon dioxide permeability coefficients (P_{CO_2}) for **1**, **2**, **5**, **5′**, and **6** were 73, 56, 80, 56, and 70 barrers, respectively. Among all the amino acid esters of EC, **5** displayed the highest CO_2 permeability, which stems presumably from the presence of an ether linkage in addition to the amino and ester functionalities because ether group is known to exhibit an affinity for CO_2 due to dipole–quadrupole interactions.[56] Despite its higher degree of esterification, the CO_2 permeability as well as the P_{CO_2}/P_{N_2} and P_{CO_2}/P_{CH_4} selectivity ratios exhibited by **5′** (DS_{Est}, 100%) were lower than those of **5** (DS_{Est}, 69%). The decrement in CO_2 permeability as well as permselectivity, accompanied by the augmentation in the density of aminoalkanoyl pendants, can be explained to arise from the enhanced hydrogen bonding and, in turn, the hindered segmental mobility and reduced chain spacing prohibiting the interaction of CO_2 molecules with polar side groups.

The most worth mentioning of the gas permeation characteristics of amino acid esters of EC (**1**, **2**, **5**, **5′**, and **6**) is the increased permselectivity for various gas pairs (Table 4). The P_{CO_2}/P_{N_2} selectivity of EC is 19, which increased up to 25 after the substitution of hydroxy groups by serine-derived appendages. Similarly, the P_{CO_2}/P_{CH_4} selectivity of EC (9.1) underwent an increase upon derivatization (10–11). The decrease in the gas permeability with a concomitant increase in the permselectivity for various gas pairs is in accordance with the well-known "tradeoff" relation.[58–62] The increased CO_2 permselectivity can be accounted for by the enhanced solubility of CO_2 in the polymer matrix probably due to the interaction of quadrupolar CO_2 molecules with the polar amino and ester moieties. The permselectivity enhancement in the present series of polymers might not appear quite significant at first glance; however, these results should be dealt with great care keeping in mind the two plausible reasons: (i) functionalization of the polymer chain could not be effected at each monomer unit as there was, on average, one hydroxy group available for derivatization per three AGUs, (ii) polar amino moieties are protected by the bulky *t*-Boc groups and therefore not exposed enough to get involved in effective interactions with CO_2 molecules. The present results imply the sensitivity of the gas transport properties of membrane-forming materials toward the modification of subtle structural features such as interchain spacing and segmental mobility.

CONCLUSIONS

This study is concerned with the synthesis of a series of *t*-Boc-protected amino acid esters of EC (**1**: DS_{Est}, 100%; **2**: DS_{Est}, 100%; **3**: DS_{Est}, 15%; **4**: DS_{Est}, 18%; **5**: DS_{Est}, 69%; **5′**: DS_{Est}, 100%; and **6**: DS_{Est}, 80%) delineating an approach to transform the thermal and gas permeation characteristics of an organosoluble cellulosic. The use of EDC·HCl as a

TABLE 4 Gas Permeability of EC, **1**, **2**, **5**, **5′**, and **6**

		P (Barrer)[a]							
Polymer	DS_{Est} (%)	He	H_2	N_2	O_2	CO_2	CH_4	P_{CO_2}/P_{N_2}	P_{CO_2}/P_{CH_4}
EC		63	96	7.8	25	146	16	19	9.1
1	100	44	60	3.6	13	73	7.0	20	10
2	100	39	48	2.4	9.5	56	4.9	23	11
5	69	35	50	3.2	12	80	7.2	25	11
5′	100	37	44	2.7	10	56	5.5	21	10
6	80	40	55	3.0	12	70	6.5	23	11

[a] 1 barrer = 1×10^{-10} cm^3 (STP) cm cm^{-2} s^{-1} $cmHg^{-1}$.

condensation agent in the presence of DMAP has been demonstrated to accomplish a facile mode of amino acid esterification of EC without any polymer chain cleavage in the course of the reaction. The bulk of the substituent on the α-carbon of the amino acid pendants was revealed to be the most significant parameter effecting the extent of substitution of the hydroxy protons of EC (DS_{Et}, 2.69), and complete incorporation of amino acid functionalities ($DS_{Est} \approx 100\%$) was observed for *t*-Boc-protected glycine and alanine in the presence of EDC·HCl. Moreover, complete esterification could also be attained for serine by using its activated ester, as evidenced by ^1H NMR. The esterification of EC with bulky organic moieties resulted in enhanced solubility in common organic solvents, notably in acetone. Fair thermal stability was revealed, and initiation of weight loss was elucidated to ensue from the degradation of *t*-butyl moieties around 200 °C in air. The amino acid functionalization of EC accompanied the lowering of glass transition temperature. Free-standing membranes were fabricated by solution casting, and the presence of polar groups led to the decreased gas permeability, due to the augmented interactions and thus reduced free volume space inside the polymer matrix, along with the improved/increased CO_2 permselectivity.

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REFERENCES AND NOTES

1 Crowley, M. M.; Schroeder, B.; Fredersdorf, A.; Obara, S.; Talarico, M.; Kucera, S.; McGinity, J. W. Int J Pharm 2004, 269, 509–522.

2 Li, X.-G.; Kresse, I.; Xu, Z.-K.; Springer, J. Polymer 2001, 42, 6801–6810.

3 Mishra, S. P. A Text Book of Fibre Science and Technology, 1st ed.; New Age International (P) Ltd.: New Delhi, 2000; Chapter 4, pp 62.

4 Klemm, D.; Philipp, B.; Heinze, T.; Heinze, U.; Wagenknecht, W. Comprehensive Cellulose Chemistry, Vols. 1, 2; Wiley-VCH: Weinheim, 1998.

5 Jones, D. In Pharmaceutical Applications of Polymers for Drug Delivery; Humphreys, S., Ed.; Rapra: UK, 2004; pp 5–7.

6 Swatloski, R., Holbrey, J., Spear, S., Rogers, R. Electrochem Soc Proc 2002, 19, 155.

7 Bodmeier, R.; Guo, X.; Paeratakul, O. In Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, 2nd ed.; McGinity, J. W., Ed.; Marcel Dekker Inc.: New York, 1997; pp 55–80.

8 Li, X.-G.; Huang, M.-R.; Gu, G.-F.; Qiu, W.; Lu, J.-Y. J Appl Polym Sci 2000, 75, 458–463.

9 Bai, S.; Sridhar, S.; Khan, A. A. J Membr Sci 2000, 174, 67–79.

10 Ravindra, R.; Sridhar, S.; Khan, A. A.; Rao, A. K. Polymer 2000, 41, 2795–2806.

11 Wang, Y.; Easteal, A. J. J Membr Sci 1999, 157, 53–61.

12 Li, X.-G.; Huang, M.-R.; Hu, L.; Lin, G.; Yang, P.-C. Eur Polym J 1999, 35, 157–166.

13 He, Y.; Yang, J.; Li, H.; Huang, P. Polymer 1998, 39, 3393–3397.

14 Li, X.-G.; Huang, M.-R. J Appl Polym Sci 1997, 66, 2139–2147.

15 Houde, A. Y.; Stern, S. A. J Membr Sci 1997, 127, 171–183.

16 Suto, S.; Niimi, T.; Sugiura, T. J Appl Polym Sci 1996, 61, 1621–1630.

17 Houde, A. Y.; Stern, S. A. J Membr Sci 1994, 92, 95–101.

18 Baughman, T. W.; Wagener, K. B. Adv Polym Sci 2005, 176, 1–42.

19 Okoshi, K.; Sakajiri, K.; Kumaki, J.; Yashima, E. Macromolecules 2005, 38, 4061–4064.

20 Vriezema, D. M.; Kros, A.; de Gelder, R.; Cornelissen, J.; Rowan, A. E.; Nolte, R. J. M. Macromolecules 2004, 37, 4736–4739.

21 Vriezema, D. M.; Hoogboom, J.; Velonia, K.; Takazawa, K.; Christianen, P. C. M.; Maan, J. C.; Rowan, A. E.; Nolte, R. J. M. Angew Chem Int Ed 2003, 42, 772–776.

22 Katsarava, R. Macromol Symp 2003, 199, 419–429.

23 Vandermeulen, G. W. M.; Tziatzios, C.; Klok, H.-A. Macromolecules 2003, 36, 4107–4114.

24 Checot, F.; Lecommandoux, S.; Gnanou, Y.; Klok, H.-A. Angew Chem Int Ed 2002, 41, 1339–1343.

25 Klok, H.-A.; Langenwalter, J. F.; Lecommandoux, S. Macromolecules 2000, 33, 7819–7826.

26 Sanda, F.; Endo, T. Macromol Chem Phys 1999, 200, 2651–2661.

27 Cornelissen, J. J. L. M.; Fischer, M.; Sommerdijk, N. A. J. M.; Nolte, R. J. M. Science 1998, 280, 1427–1430.

28 Scholl, M.; Nguyen, T. Q.; Bruchmann, B.; Klok, H.-A. J Polym Sci Part A: Polym Chem 2007, 45, 5494–5508.

29 Deng, C.; Chen, X.; Sun, J.; Lu, T.; Wang, W.; Jing, X. J Polym Sci Part A: Polym Chem 2007, 45, 3218–3230.

30 Biagini, S. C. G.; Parry, A. L. J Polym Sci Part A: Polym Chem 2007, 45, 3178–3190.

31 Sinaga, A.; Ravi, P.; Hatton, T. A.; Tam, K. C. J Polym Sci Part A: Polym Chem 2007, 45, 2646–2656.

32 Carrillo, A.; Yanjarappa, M. J.; Gujraty, K. V.; Kane, R. S. J Polym Sci Part A: Polym Chem 2006, 44, 928–939.

33 Ayres, L.; Hans, P.; Adams, J.; Löwik, D. W. P. M.; van Hest, J. C. M. J Polym Sci Part A: Polym Chem 2005, 43, 6355–6366.

34 Klok, H.-A. J Polym Sci Part A: Polym Chem 2005, 43, 1–17.

35 Maynard, H. D.; Okada, S. Y.; Grubbs, R. H. J Am Chem Soc 2001, 123, 1275–1279.

36 Maynard, H. D.; Okada, S. Y.; Grubbs, R. H. Macromolecules 2000, 33, 6239–6248.

37 Biagini, S. C. G.; Coles, M. P.; Gibson, V. C.; Giles, M. R.; Marshall, E. L.; North, M. Polymer 1998, 39, 1007–1014.

38 Nakagawa, T.; Fujiwara, Y.; Minoura, N. J Membr Sci 1984, 18, 111–127.

39 Khan, F. Z.; Shiotsuki, M.; Sanda, F.; Nishio, Y.; Masuda, T. J Polym Sci Part A: Polym Chem 2008, 46, 2326–2334.

40 Khan, F. Z.; Shiotsuki, M.; Nishio, Y.; Masuda, T. J Membr Sci 2008, 312, 207–216.

41 Jinqing, Q.; Khan, F. Z.; Satoh, M.; Wada, J.; Hayashi, H.; Mizoguchi, K.; Masuda, T. Polymer 2008, 49, 1490–1496.

42 Khan, F. Z.; Shiotsuki, M.; Nishio, Y.; Masuda, T. Macromolecules 2007, 40, 9293–9303.

43 Morita, R.; Khan, F. Z.; Sakaguchi, T.; Shiotsuki, M.; Nishio, Y.; Masuda, T. J Membr Sci 2007, 305, 136–145.

44 Khan, F. Z.; Sakaguchi, T.; Shiotsuki, M.; Nishio, Y.; Masuda, T. Macromolecules 2006, 39, 9208–9214.

45 Khan, F. Z.; Sakaguchi, T.; Shiotsuki, M.; Nishio, Y.; Masuda, T. Macromolecules 2006, 39, 6025–6030.

46 Masuda, T.; Iguchi, Y.; Tang, B.-Z.; Higashimura, T. Polymer 1988, 29, 2041–2049.

47 Zhang, C.; Price, L. M.; Daly, W. H. Biomacromolecules 2006, 7, 139–145.

48 Newkome, G. R.; Weis, C. D.; Abourahma, H. ARKIVOC 2000, 1, 210–217.

49 Depuy, C. H.; King, R. W. Chem Rev 1960, 60, 431–457.

50 Stevens, M. P. Polymer Chemistry: An Introduction, 3rd ed.; Oxford University Press: New York, 1999; Chapter 4, pp 70–74.

51 Katsumata, T.; Maitani, M.; Huang, C.-C.; Shiotsuki, M.; Masuda, T. Polymer 2008, 49, 2808–2816.

52 Senthilkumar, U.; Reddy, B. S. R. J Membr Sci 2007, 292, 72–79.

53 Kono, T.; Sakaguchi, T.; Hu, Y.; Shiotsuki, M.; Sanda, F.; Masuda, T. J Polym Sci Part A: Polym Chem 2006, 44, 5943–5953.

54 Lin, H.; Freeman, B. D. J Mol Struct 2005, 739, 57–74.

55 Shida, Y.; Sakaguchi, T.; Shiotsuki, M.; Sanda, F.; Freeman, B. D.; Masuda, T. Macromolecules 2005, 38, 4096–4102.

56 Lin, H.; Freeman, B. D. J Membr Sci 2004, 239, 105–117.

57 Ghosal, K.; Chern, R. T.; Freeman, B. D.; Daly, W. H.; Negulescu, I. I. Macromolecules 1996, 29, 4360–4369.

58 Robeson, L. M. J Membr Sci 2008, 320, 390–400.

59 Freeman, B. D. Macromolecules 1999, 32, 375–380.

60 Robeson, L. M.; Burgoyne, W. F.; Langsam, M.; Savoca, A. C.; Tien, C. F. Polymer 1994, 35, 4970–4978.

61 Koros, W. J.; Fleming, G. K. J Membr Sci 1993, 83, 1–80.

62 Robeson, L. M. J Membr Sci 1991, 62, 165–185.