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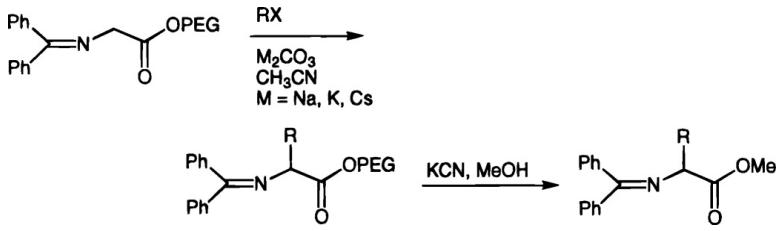

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Soluble Polymer Supported Synthesis of α-Amino Acid Derivatives

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A Schiff base activated glycine supported on a soluble polymer (poly(ethylene glycol) (PEG)) was readily alkylated with a wide variety of electrophiles in the presence of a carbonate base in acetonitrile. The presence of the polymer provided a phase-transfer catalysis environment which accelerated the reaction. Effects of various carbonate bases and leaving groups have been also studied. Completion of the PEG-supported reaction was obtained without using a large excess of reagents or an extra phase-transfer catalyst, even in the case of unreactive or hindered electrophiles. After cleavage from the polymer, α-amino esters are obtained in good yields.

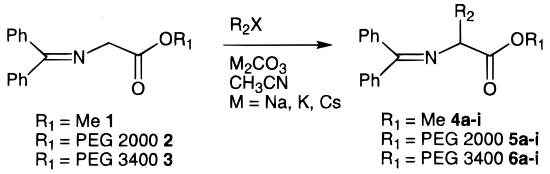
Introduction

Combinatorial chemistry has emerged as a powerful technology to generate large numbers of molecules.[1] One widely used technique in combinatorial chemistry is the solid-phase organic synthesis (SPOS). Molecules are synthesized on an insoluble solid support where reactions are driven to completion by using excess of reagents which can be removed by washing with various solvents. Nevertheless, inherent problems on an insoluble polymer are reactive site accessibility, site−site interaction, and monitoring of the reaction.[2,15a]

One alternative to the SPOS is the liquid-phase organic synthesis (LPOS) where soluble polymers such as poly(ethylene glycol) (PEG) are utilized as supports.[3] The PEG support solubilizes the reacting center in the reaction solvent. After completion of the reaction, purification is performed by precipitation, filtration, and washing of the polymer. Characterization of the polymer supported molecule is performed without preliminary cleavage of the growing structure including solution NMR and mass spectrometry.[4]

We present here our results on the synthesis of α-amino acid derivatives by alkylation of a Schiff base activated glycine supported on a poly(ethylene glycol).[5a] Various factors that can affect the efficiency of this reaction have been studied. We are showing also that positive effects on the reactivity of the reacting center can be exerted by the polymer support.

Since from an economical and practical point of view, phase-transfer catalyzed reactions are attractive,[6] we have recently adapted an efficient and facile alkylation method initially developed for the synthesis in solution of α-amino acids using a mild carbonate base such as K_2CO_3 on poly(ethylene glycol) (eq 1).[7] To proceed in a reasonable amount of time in solution, this solid−liquid phase-transfer reaction



(1)

requires the use of a phase-transfer catalyst such as a quaternary ammonium salt. We showed that the presence of a PEG support is beneficial for the kinetics of the reaction and that adding an external catalyst is not necessary. We describe here the synthesis of a wide variety of α-aminoesters accessible with this method which could be useful in combinatorial chemistry.

Results

The reaction of Schiff base activated glycine esters **1**−**3** has been systematically studied in the presence of various carbonate bases, of PEG supports of two different sizes, and of diverse electrophiles. One of the main advantage of soluble polymers is that the analysis of the completion of the reaction can be easily determined by ^{1}H NMR. Consequently, samples were taken regularly and analyzed, and the conversion of the starting material into the expected product was calculated.

The starting material was synthesized as described in eq 2. Both of the hydroxyl groups of the polymer PEG 2000 (respectively PEG 3400) were esterified with Boc glycine using DCC, DMAP as coupling agent to yield **7** (respectively **8**).[8] The Boc group was cleaved with HCl gas in CH_2Cl_2. Transimination of the resulting hydrochloride **9** (respectively **10**) with benzophenone imine yielded the starting material **2** (respectively **3**).[9] All these reactions went to completion, and this was checked by ^{1}H NMR.

In the preliminary experiments that were designed, a bifunctional PEG with an average molecular weight of 2000 was used as a support to increase the loading of the resin compared to the more commonly used monofunctional HO-

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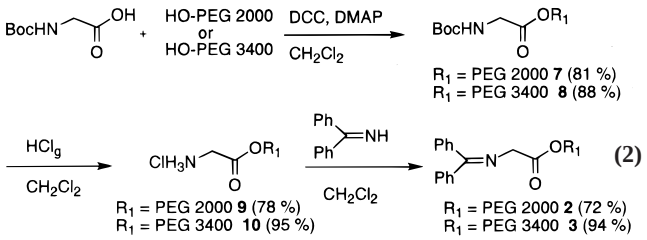
Table 1. Reaction Time for Alkylation of **1**−**3** with *n*-BuBr in the Presence of Various Bases[a]

base	**1** (h)	**2** (h)	**3** (h)	**1** + PEG-OMe 2000 (h)	**1** + PEG-OMe 3400 (h)
Na_2CO_3		>48 (16%)[b]			
K_2CO_3	>48 (46%)[b]	32	32	32	26
Cs_2CO_3	6	3	3	3	1

[a] Experimental conditions: 1 equiv of activated methylene, 1.5 equiv of *n*-BuBr, 3 equiv of base in refluxing CH_3CN. [b] The number in parentheses corresponds to the conversion reached after 48 h of reaction.



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PEG-OMe 5000.[3] It was noticed by others[10] and by our group[5b] that in order to achieve a reasonable balance between loading and good precipitation properties, it was preferable to use a bifunctional PEG 3400-OH. The bifunctional PEG 2000-OH is often more difficult to precipitate than higher molecular weight polymer, and this probably accounts for less recovery of material and lower yields (eq 2). Bifunctional PEG 3400 was then preferred from a synthetic point of view, but since we had both families of molecules in hand (PEG 2000 and PEG 3400), we studied the influence of the polymer according to their size.

As a test reaction, we studied the alkylation of Schiff bases **1**−**3** with a poor alkylating agent such as *n*-BuBr with different carbonate bases (eq 1, R_2X = *n*-BuBr, M_2CO_3, M = Na, K, or Cs). The acceleration due to the PEG could be demonstrated by comparing the reaction completion time of three different experiments: one in the absence of PEG (reaction of Schiff base **1**), one with the PEG supported Schiff base (reaction of **2** and **3**), and one with Schiff base **1** using a PEG dimethyl ether as an external catalyst in the same molecular ratio.

The results are summarized in Table 1.

In all cases, the reaction in the presence of a PEG molecule was dramatically faster than the reaction in the absence of polymer: in the case of Schiff base **1** without external catalyst only 46% of conversion was obtained after 48 h with K_2CO_3. In the presence of PEG, the reaction with K_2CO_3 was complete in all cases after 32 h. Using Cs_2CO_3[11] as a base, the reaction time was also shorter in the presence of PEG (3 h vs 6 h).

In the case of the PEG supported reactions, the acceleration took place for both polymer sizes. When PEG-OMe was used as an external catalyst, the reaction was faster with PEG-3400. We also compared the PEG to more classical phase-transfer catalysts such as *n*-Bu_4NBr or 18-crown-6. In both cases the reaction was faster but the yields were lower (78% yield in 14 h using *n*-Bu_4NBr, 65% yield in 4 h using 18-crown-6).

Table 2. Reaction Time for Alkylation of **1**−**3** with *n*-BuX (X = I, Br, Cl)[a]

	1 (h)		**3** (h)	
electrophile	K_2CO_3	Cs_2CO_3	K_2CO_3	Cs_2CO_3
n-BuCl	>48 (4%)[b]	32	>48 (54%)[b]	6
n-BuBr	>48 (46%)[b]	6	32	3
n-BuI	>48 (65%)[b]	2	28	0.5

[a] Experimental conditions: 1 equiv of activated methylene, 1.5 equiv of *n*-BuX, 3 equiv of base in refluxing CH_3CN. [b] The number in parentheses corresponds to the conversion reached after 48 h of reaction.

Table 3. Alkylation of Schiff Base **3** with Various Electrophiles in the Presence of Cs_2CO_3[a]

6	R-X	Reaction time (reflux)	yield of **6** (%) (reflux)	Reaction time (RT)	yield of **6** (%) (RT)	yield of **4** (%)
a	*n*-Bu-I	0.5 h	92	4h	89	_c
a	*n*-BuBr	3h	97	6h	85	78
a	*n*-BuCl	6h	81	8h	79	_c
b	$PhCH_2Br$	1h	91	2h	88	64
b	$PhCH_2Cl$	1h[b]	79	8h	78	_c
c		3h	98	4h	84	68
d		3h	97	4h	88	76
e		3h	88	_c	_c	84
f		2h	82	_c	_c	70
g	$Ph(CH_2)_2Br$	2h	77	_c	_c	79
h		8h	75	_c	_c	66
i		6h	91	_c	_c	98

[a] Experimental conditions: 1 equiv of activated methylene, 1.5 equiv of *n*-BuX, 3 equiv of Cs_2CO_3 in CH_3CN. [b] This reaction was performed on PEG 2000 as support. [c] Not performed.

In all cases, the reaction was faster using Cs_2CO_3 as a base. None of the reactions with Na_2CO_3 went to completion, and consequently we did not further investigate reactions with this base.

Since another key variable of these reactions was the nature of the leaving group, we studied the reaction of unreactive *n*-butyl halides in the presence of K_2CO_3 or Cs_2CO_3 (Table 2).

In the absence of PEG, none of the reactions of **1** in the presence of K_2CO_3 went to completion while the reaction of **3** went to completion in the case of bromine or iodine as leaving groups. With Cs_2CO_3, completion of the reaction of **1** could be reached with the chloride derivative in 32 h and reduced to 6 h when the reaction was supported on PEG. Since bromide and iodide reacted much faster (3 h and 0.5 h, respectively), an alternative was to perform the reaction at room temperature instead of refluxing acetonitrile. These results as well as examples of more reactive electrophiles are presented in Table 3.

A wide variety of electrophiles was used in the alkylation reaction. The strong electrophiles such as benzyl, propargyl,

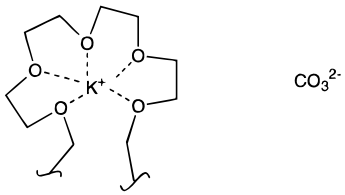
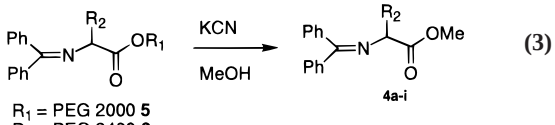


Figure 1.

or allyl halides reacted rapidly, and the reaction was complete within either 1−3 h in refluxing acetonitrile (entry **b**−**e**) or 2−8 h at room temperature (entry **b**−**d**). More hindered electrophiles such as secondary hexyl iodide (entry **h**) and methyl-3-bromo-2-methylpropionate (entry **i**) needed 6−8 h to completely react in refluxing acetonitrile. 2-Phenylethyl bromide (entry **g**) prone to β-elimination yielded the expected alkylated product **6g** without side reaction.

The α-amino esters synthesized by this method could be used for further reaction on soluble polymer support.[5b,12] Another possibility was to cleave the protected α-amino acid from the polymer by transesterification in the presence of KCN (eq 3).[13] In Table 3 are presented the yields corresponding to the cleavage obtained from PEG 3400 supported molecules.



(3)

Discussion

PEGs are open chain polyethers which have shown an activity as phase transfer catalysts in a wide variety of reactions.[14] In the alkylation reaction that we presented, an acceleration due to the presence of the polymer had been noticed and consequently it was not necessary to use an extra catalyst such as a quaternary ammonium salt in order to reach completion of the reaction. Probably the PEG support acts as a stoichiometric catalyst in this solid−liquid phase-transfer reaction. Alternating oxygen atoms present in the polymer provides cation coordination, solubilizing at least partially the inorganic base in the solvent and enhancing the strength of the anion, in a way comparable to the complexation of a cation by a crown ether (Figure 1).

Nevertheless, this influence is not as effective as the one obtained with a crown ether such as 18-crown-6. However, from a practical, economical, and toxicity point of view, PEG-OMe is a good choice for use as an external catalyst.

It has been proposed recently that supports used in solid-phase synthesis are like solvents, and thorough studies have shown that for a given reaction the reaction rate could depend on the nature of the resin support.[15] To our knowledge, although the effect of the resins in the solid phase have been studied, there are few examples dealing with the influence of the polymer on a poly(ethylene glycol) supported substrate. Bayer et al.[16a] described the acceleration in PEG supported peptide coupling. Bergbreiter et al.[16b] noticed that in some cases a PEG support can act as a macromolecular protection in a hydrogenation reaction. Metha et al.[16c] described a positive dual effect of the PEG support for scandium promoted cleavage of a sugar molecule from the polymer. A similar accelerating effect has been described in a Heck reaction.[5b,16d]

The supported reactions on PEG 2000 or PEG 3400 have a similar rate positive effect independent of their size. It is commonly accepted that in some reactions only one cation at a time is coordinated and transferred in the solvent by one molecule of PEG.[17] Therefore, this process does not depend on the size of the polymer. Nevertheless, this cannot be generalized to the whole family of PEGs since we have been studying this effect on two PEGs of similar sizes. However, since mechanical loss of PEG 2000 supported molecules was higher, PEG 3400 was chosen as the preferred support.

The reaction of PEG 3400-OMe as an external catalyst was faster than for the supported reaction. One explanation could be that PEG 3400-OMe is a better catalyst than **3** in this reaction but we did not investigate this point in detail.

The results of the alkylation reaction showed that the method developed here is very mild, efficient, and versatile. Cs_2CO_3 proved to be the base of choice in these alkylation reactions. A wide variety of alkylating agent can be used, and it is noteworthy that, in sharp contrast to the corresponding reaction in the solid phase on a Wang resin,[18] it was not necessary to use excess reagents in order to obtain completion of the reaction in a reasonable amount of time. Basically, 1.5 equiv of electrophile per activated methylene were employed, but one can go as low as 1.1 equiv to obtain the same result. Even in the case of very unreactive or hindered electrophiles, reaction went to completion without using a large excess of alkylating agents or an extra phase-transfer catalyst. Furthermore, this method is also cost-effective since one can consider working with chlorides instead of more expensive or less available (at least industrially) bromides and iodides. Also, this reaction does not require the use of expensive base or sophisticated conditions even if they are also effective.[19]

In conclusion, we have developed an efficient synthesis of PEG supported α-amino esters which could be useful in combinatorial chemistry.

Experimental Section

General. All reagents were obtained from Aldrich Chemical Co. and used without purification. ^{1}H and ^{13}C NMR analyses were performed, respectively, with a Brüker Advance DPX-200 and 400 MHz spectrometer. Infrared spectra were recorded on a Perkin-Elmer FT-IR spectrometer Paragon 1000, taken as a micro cup of KBr by diffuse reflectance, and only characteristic absorptions were reported. Mass spectra (electrospray ionization mode ESIMS) were taken on a Platform II (Micromass, Manchester, U.K.) quadrupole mass spectrometer fitted with an electrospray interface. We report the mass spectrometry for PEG 3400 only. The mass spectrometer was calibrated in the positive-ion ESI mode. The samples were dissolved in H_2O/CH_3CN (50/50 in vol.). Multiprotonated ions were recovered in the positive mode. PEG 3400 supported molecules appeared as distributions corresponding to charge states ranging from +2 to +5, and oligomers between $n = 74$ to $n = 88$ were

detected. Only one significant peak was reported corresponding to $n = 75$ or $n = 80$ when the sample was triply (noted +3) or quadruply (noted +4) protonated, and we used the increment of mass between the product and the PEG 3400 to confirm the spectrum. Correlations between the calculated and measured values were observed in both of the protonation states considered.

Poly(ethylene glycol)-2000 Di(*tert*-butyloxycarbonylglycinate) (7). A mixture of poly(ethylene glycol)-2000 (40.0 g, 20 mmol), *tert*-butyloxycarbonyl glycine (7.0 g, 40 mmol), and DMAP (4.9 g, 40 mmol) in 200 mL of CH_2Cl_2 was cooled to 0 °C. After 10 min, DCC (8.2 g, 40 mmol) was added. The reaction mixture was stirred for 14 h at room temperature. The precipitate of DCU was filtered, and the solution was concentrated and precipitated in Et_2O. The product was filtered and dried in vacuo to yield 37.6 g (81%) of the title compound: IR (KBr) 2872 (m), 1710 (s), 1526 (m), 1223 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.45 (s, 9H), 3.50−3.70 (s large, ≈180H), 3.95−4.05 (m, 2H), 4.25−4.35 (m, 2H), 5.05−5.15 (m, 1H).

Poly(ethylene glycol)-3400 Di(*tert*-butyloxycarbonylglycinate) (8). The same procedure as that for the synthesis of **7** was used with poly(ethylene glycol)-3400 (17.0 g, 5 mmol), *tert*-butyloxycarbonyl glycine (1.75 g, 10 mmol), and DMAP (0.30 g, 1 mmol) in 100 mL of CH_2Cl_2 to yield 17.5 g (94%) of the title compound: IR (KBr) 2881 (m), 1718 (s), 1499 (m), 1260 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.45 (s, 9H), 3.50−3.80 (s large, ≈310H), 3.95−4.05 (m, 2H), 4.25−4.35 (m, 2H), 5.05−5.15 (m, 1H); MS (Electrospray) *m*/*z*, $n = 75$, 1220.53 (+3), $n = 80$, 970.52 (+4).

Poly(ethylene glycol)-2000 Di(glycinate hydrochloride) (9). HCl gas was bubbled through a solution of **7** (39.8 g, 17.2 mmol) in 200 mL of CH_2Cl_2 for 4 h. HCl was evaporated, CH_2Cl_2 was added and evaporated, and this was repeated three times. The solution was precipitated in Et_2O and the product filtered and dried in vacuo to yield 29.4 g (78%) of the title compound: IR (KBr) 3418 (s), 2876 (m), 1752 (m), 1106 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.50−3.70 (s large, ≈180H), 3.90−4.05 (m, 2H), 4.35−4.45 (m, 2H).

Poly(ethylene glycol) 3400 Di(glycinate hydrochloride) (10). The same procedure as for the synthesis of **9** was used with **8** (16.17 g, 4.35 mmol) in 100 mL of CH_2Cl_2, to yield 15.5 g (99%) of the title compound: IR (KBr) 3340 (m), 2868 (m), 1750 (s), 1100 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.50−3.70 (s large, ≈310H), 3.90−4.05 (m, 2H), 4.35−4.45 (m, 2H); MS (Electrospray) *m*/*z*, $n = 75$, 1161.01 (+3), $n = 80$, 915.59 (+4).

Methyl *N*-(Diphenylmethylene)glycinate (1).[9] A mixture of glycine methyl ester hydrochloride (2 g, 15.9 mmol) and benzophenone imine (2.88 g, 15.9 mmol) was stirred in 50 mL of CH_2Cl_2 under argon at room temperature for 24 h. The precipitate of NH_4Cl was filtered, and the filtrate was concentrated, taken up in 50 mL of Et_2O, washed with 50 mL of water, and dried over $MgSO_4$. Recrystallization from Et_2O/hexane yielded 3.58 g (89%) of the title compound: IR (KBr) 3120 (m), 1748 (m), 1616 (s), 1184 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.70 (s, 3H), 4.20 (s, 2H), 7.20−7.60 (m, 10H).

Poly(ethylene glycol)-2000 Di(*N*-(diphenylmethylene)glycinate) (2). A mixture of **9** (22.7 g, 10.37 mmol) and benzophenone imine (3.8 g, 21.75 mmol) in 300 mL of CH_2Cl_2 was stirred for 24 h at room temperature. The precipitate of NH_4Cl was filtered, and the filtrate was concentrated and purified by precipitation of the product in Et_2O, filtration, and drying in vacuo to yield 18.2 g (71.6%) of the title compound: IR (KBr) 2872 (m), 1744 (m), 1627 (m), 1140 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.50−3.70 (s large, ≈180H), 4.20 (s, 2H), 4.25−4.35 (m, 2H), 7.20−7.70 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 55.92, 62.09, 64.36, 66.23, 69.44, 70.74−70.96, 72.93, 128.45, 128.68, 128.90, 129.11, 129.16, 130.44, 130.87, 132.82, 136.35, 137.97, 139.61, 170.99, 172.31.

Poly(ethylene glycol)-3400 Di(*N*-(diphenylmethylene)glycinate) (3). The same procedure as that for the synthesis of **2** was used starting from **10** (7.17 g, 2 mmol) and benzophenone imine (0.73 g, 4 mmol) in 100 mL of CH_2Cl_2 to yield 7.24 g (94%) of the title compound: IR (KBr) 2876 (m), 1738 (m), 1634 (m), 1138 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.50−3.70 (s large, ≈310H), 4.20 (s, 2H), 4.25−4.35 (m, 2H), 7.15−7.75 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 55.85, 64.30, 69.35, 70.66−70.89, 127.96, 128.39, 129.07, 129.21, 130.82, 136.25, 139.53, 170.87, 172.21; MS (Electrospray) *m*/*z*, $n = 75$, 1263.27 (+3), $n = 80$, 996.91 (+4).

Methyl 2-(*N*-(Diphenylmethylene amino))hexanoate (4a). A mixture of **1** (0.064 g, 0.25 mmol), butyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN was refluxed for the indicated time. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, and filtered. Then, in the case of poly(ethylene glycol)-OMe used as catalyst, the solution was precipitated in Et_2O and the filtrate was dried in vacuo. When *n*-Bu_4NBr or 18-C-6 were used as catalyst, the CH_2Cl_2 solution was filtered and the filtrate was washed three times with water, dried on $MgSO_4$, concentrated, and dried in vacuo.

(a) With BuBr (0.05 g), K_2CO_3 (0.11 g): The reaction was not complete after 48 h of refluxing.

(b) With BuBr (0.05 g), K_2CO_3 (0.11 g), poly(ethylene glycol)-2000-OMe (0.5 equiv, 0.25 g): The reaction mixture was refluxed for 32 h to yield 0.065 g (85%) of the title compound: IR (neat) 2854 (m), 1731 (s), 1626 (m), 1277 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, $J = 6.5$ Hz, 3H), 1.15−1.35 (m, 4H), 1.85−1.95 (m, 2H), 3.35−3.45 (m, 2H), 3.70 (s, 3H), 4.15−4.25 (m, 1H), 7.20−7.80 (m, 10H).

(c) With BuBr (0.05 g), K_2CO_3 (0.11 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for 26 h to yield 0.064 g (83%) of the title compound.

(d) With BuBr (0.05 g), K_2CO_3 (0.11 g), *n*-Bu_4NBr (1 equiv, 0.081 g):[7] The reaction mixture was refluxed for 14 h to yield 0.060 g (78%) of the title compound.

(e) With BuBr (0.05 g), K_2CO_3 (0.11 g), 18-crown-6 (1 equiv, 0.066 g): The reaction mixture was refluxed for 4 h to yield 0.050 g (65%) of the title compound.

(f) With BuBr (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 6 h to yield 0.073 g (94%) of the title compound.

(g) With BuBr (0.05 g), Cs_2CO_3 (0.24 g), poly(ethylene glycol)-2000-OMe (0.5 equiv, 0.25 g): The reaction mixture was refluxed for 2 h to yield 0.070 g (91%) of the title compound.

(h) With BuBr (0.05 g), Cs_2CO_3 (0.24 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for 1 h to yield 0.077 g (98%) of the title compound.

(i) With BuI (0.07 g), K_2CO_3 (0.11 g): The reaction was not complete after 48 h of refluxing.

(j) With BuI (0.07 g), K_2CO_3 (0.11 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for 2 h to yield 0.068 g (88%) of the title compound.

(k) With BuI (0.07 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 2 h to yield 0.073 g (95%) of the title compound.

(l) With BuI (0.07 g), Cs_2CO_3 (0.24 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for $^1/_2$ h to yield 0.077 g (98%) of the title compound.

(m) With BuCl (0.04 g), K_2CO_3 (0.11 g): The reaction was not complete after 48 h of refluxing.

(n) With BuCl (0.04 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 32 h to yield 0.065 g (84%) of the title compound.

Poly(ethylene glycol)-2000 Di(2(*N*-(diphenylmethylene-amino))hexanoate) (5a). A heterogeneous mixture of **2** (0.31 g, 0.125 mmol), butyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN was refluxed for the indicated time. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo.

(a) With BuBr (0.05 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 32 h to yield 0.24 g (74%) of the title compound: IR (KBr) 2868 (m), 1736 (s), 1363 (m), 1142 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.85 (t, $J = 7.0$ Hz, 3H), 1.10−1.70 (m, 4H), 1.85−2.00 (m, 2H), 3.50−3.70 (s large, ≈180H), 4.05−4.15 (m, 1H), 4.20−4.35 (m, 2H), 7.15−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.33, 22.77, 28.46, 33.65, 61.89, 64.27, 65.70, 69.29, 70.07−70.87, 73.00, 128.23, 128.39, 128.86, 128.97, 129.14, 130.63, 136.82, 139.93, 142.95, 170.67, 172.73.

(b) With BuI (0.07 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 28 h to yield 0.29 g (91%) of the title compound.

(c) With BuCl (0.04 g), K_2CO_3 (0.11 g): The reaction was not complete after 48 h of refluxing.

(d) With BuBr (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 3 h to yield 0.27 g (84%) of the title compound.

(e) With BuI (0.07 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for $^1/_2$ h to yield 0.31 g (97%) of the title compound.

(f) With BuCl (0.04 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 6 h to yield 0.25 g (78%) of the title compound.

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene amino))hexanoate) (6a). The same procedure as for the synthesis of **5a** was used with **3** (0.48 g, 0.125 mmol), butyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN.

(a) With BuBr (0.05 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 32 h to yield 0.45 g (92%) of the title compound: IR (KBr) 2872 (m), 1739 (s), 1358 (m), 1112 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.85 (t, $J = 7.0$ Hz, 3H), 1.10−1.70 (m, 4 H), 1.85−2.00 (m, 2H), 3.50−3.80 (s large, ≈310H), 4.05−4.15 (m, 1H), 4.20−4.35 (m, 2H), 7.15−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14,-35, 19,27, 22,80, 28,49, 31,02, 33,67, 62,07, 64,30, 65,72, 67,19, 68,29, 69,41, 70,44−71,74, 72,94, 128,26, 128,41, 128,88, 128,97, 129,16, 130,64, 136,86, 139,96, 170,67, 172,-75; MS (Electrospray) *m/z*, $n = 75$, 1307.64 (+3), $n = 80$, 1025.16 (+4).

(b) With BuBr (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 3 h to yield 0.48 g (97%) of the title compound.

(c) With BuBr (0.05 g), Na_2CO_3 (0.08 g): The reaction was not complete after 48 h of refluxing.

(d) With BuI (0.07 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 28 h to yield 0.43 g (87%) of the title compound.

(e) With BuCl (0.04 g), K_2CO_3 (0.11 g): The reaction was not complete after 48 h of refluxing.

(f) With BuI (0.07 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for $^1/_2$ h to yield 0.455 g (92%) of the title compound.

(g) With BuCl (0.04 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 6 h to yield 0.40 g (81%) of the title compound.

(h) With BuBr (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was stirred at room temperature for 6 h to yield 0.42 g (85%) of the title compound.

(i) with BuI (0.07 g), Cs_2CO_3 (0.24 g): The reaction mixture was stirred at room temperature for 4 h to yield 0.44 g (89%) of the title compound.

(j) With BuCl (0.04 g), Cs_2CO_3 (0.24 g). The reaction mixture was stirred at room temperature for 8 h to yield 0.39 g (79%) of the title compound.

Methyl *N*-(Diphenylmethylene)phenylalaninate (4b). A mixture of methyl *N*-(diphenylmethylene)-glycinate **1** (0.064 g, 0.25 mmol), benzyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN was refluxed for the indicated time. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, and filtered. Then, in the case of poly(ethylene glycol)-OMe as catalyst, the filtrate was precipitated in Et_2O, the solution was evaporated, and the product was dried in vacuo.

(a) With $PhCH_2Br$ (0.06 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 24 h to yield 0.076 g (89%) of the title compound: IR (neat) 2869 (m), 1718 (s), 1676 (m), 1141 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.15−3.25 (m, 2H), 3.75 (s, 3H), 4.20−4.30 (dd, $J_1 = 9$ Hz, $J_2 = 4.5$ Hz, 1H), 6.55−6.65 (m, 2H), 7.10−7.70 (m, 13H).

(b) With $PhCH_2Br$ (0.06 g), K_2CO_3 (0.11 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for 24 h to yield 0.082 g (96%) of the title compound.

(c) With $PhCH_2Br$ (0.06 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 3 h to yield 0.081 g (94%) of the title compound.

(d) With $PhCH_2Br$ (0.06 g), Cs_2CO_3 (0.24 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for $^1/_2$ h to yield 0.084 g (98%) of the title compound.

(e) With $PhCH_2Cl$ (0.05 g), K_2CO_3 (0.11 g): The reaction was not complete after 32 h of refluxing.

(f) With $PhCH_2Cl$ (0.05 g), K_2CO_3 (0.11 g), poly(ethylene glycol)-3400-OMe (0.5 equiv, 0.43 g): The reaction mixture was refluxed for 24 h to yield 0.073 g (85%) of the title compound.

(g) With $PhCH_2Cl$ (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 1 h to yield 0.068 g (79%) of the title compound.

Poly(ethylene glycol)-2000 Di(*N*-(diphenylmethylene)-phenylalaninate) (5b). A heterogeneous mixture of **2** (0.31 g, 0.125 mmol), benzyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN was refluxed for the indicated time. After cooling, the base was filtered, the filtrate was concentrated, dissolved in CH_2Cl_2, filtered and then, precipitated in Et_2O. The product was filtered and dried in vacuo.

(a) With $PhCH_2Br$ (0.06 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 6 h to yield 0.245 g (74%) of the title compound: IR (KBr) 2870 (m), 1740 (s), 1658 (m), 1140 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.10−3.25 (m, 2H), 3.50−3.70 (s large, ≈180H), 4.15−4.25 (m, 2H), 4.25−4.35 (m, 1H), 6.55−7.65 (m, 15H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.93, 61.87, 64.54, 67.52, 69.37, 70.08−71.70, 72.92, 126.68, 128.22, 128.37, 128.49, 128.53, 128.67, 128.72, 128.85, 128.92, 129.13, 129.24, 129.69, 129.78, 130.25, 130.65, 136.43, 138.30, 139.74, 171.31, 172.03.

(b) With $PhCH_2Cl$ (0.05 g), K_2CO_3 (0.11 g): The reaction mixture was refluxed for 10 h to yield 0.22 g (67%) of the title compound.

(c) With $PhCH_2Br$ (0.06 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 1 h to yield 0.31 g (94%) of the title compound.

(d) With $PhCH_2Cl$ (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 1 h to yield 0.26 g (79%) of the title compound.

Poly(ethylene glycol)-3400 Di(*N*-(diphenylmethylene)-phenylalaninate) (6b). The same procedure as for the synthesis of **5b** was used with **3** (0.48 g, 0.125 mmol), benzyl halide (0.375 mmol), and inorganic base (0.75 mmol) in 10 mL of CH_3CN.

(a) With $PhCH_2Br$ (0.06 g), Cs_2CO_3 (0.24 g): The reaction mixture was refluxed for 1 h to yield 0.46 g (91%) of the title compound: IR (KBr) 2870 (m), 1734 (s), 1662 (m), 1276 (s), 1140 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.10−3.25 (m, 2H), 3.50−3.70 (s large, ≈310H), 4.15−4.25 (m, 2H), 4.25−4.35 (m, 1H), 6.55−7.65 (m, 15H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.92, 61.70, 64.53, 67.50, 69.35, 70.35−70.97, 72.90, 126.68, 128.02, 128.36, 128.53, 128.72, 129.11, 130.23, 130.64, 136.40, 138.28, 139.72, 171.29, 172.01; MS (Electrospray) *m*/*z*, $n = 75$, 1330.25 (+3), $n = 80$, 1042.10 (+4).

(b) With $PhCH_2Br$ (0.06 g), Cs_2CO_3 (0.24 g): The reaction mixture was stirred at room temperature for 2 h to yield 0.44 g (88%) of the title compound.

(c) With $PhCH_2Cl$ (0.05 g), Cs_2CO_3 (0.24 g): The reaction mixture was stirred at room temperature for 8 h to yield 0.39 g (78%) of the title compound.

Poly(ethylene glycol)-2000 Di(2(*N*-(diphenylmethylene-amino))-4-pentenoate (5c). Allyl bromide (0.18 g, 1.5 mmol) was added to **2** (1.22 g, 0.5 mmol) and potassium carbonate (0.42 g, 3 mmol) in 20 mL of CH_3CN. The mixture was refluxed for 14 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.97 g (77%) of the title compound: IR (KBr) 2868 (m), 1735 (s), 1652 (m), 1126 (s), 956 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.60−2.70 (m, 2H), 3.50−3.70 (s large, ≈180H), 4.10−4.20 (m, 1H), 4.25−4.35 (m, 2H), 4.90−5.10 (m, 2H), 5.60−5.80 (m, 1H), 7.20−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 38.42, 61.12, 64.44, 65.54, 69.42, 70.07−70.92, 72.25, 118.06, 128.06, 128.36, 128.43, 128.69, 128.91, 129.07, 129.17, 129.24, 130.46, 130.75, 132.83, 134.72, 136.76, 139.94, 171.09, 172.11.

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene-amino))-4-pentenoate) (6c). Allyl bromide (0.05 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 3 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.48 g (98%) of the title compound: IR (KBr) 2871 (m), 1736 (s), 1655 (m), 1137 (s), 948 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.60−2.70 (m, 2H), 3.50−3.80 (s large, ≈310H), 4.15−4.25 (m, 1H), 4.25−4.35 (m, 2H), 4.95−5.15 (m, 2H), 7.15−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 38.35, 61.95, 64.38, 65.48, 69.35, 70.51−70.91, 72.93, 118.01, 128.30, 128.37, 128.87, 129.02, 129.17, 130.69, 134.67, 136.70, 139.88, 171.01, 171.99; MS (Electrospray) *m*/*z*, $n = 75$, 1297.08 (+3), $n = 80$, 1022.60 (+4).

The same procedure as that for the synthesis of **6c** was used in the same proportions, and the mixture was stirred at room temperature for 4 h to yield 0.41 g (84%) of the title compound.

Poly(ethylene glycol)-2000 Di(2(*N*-(diphenylmethylene-amino))-4-pentynoate) (5d). Propargyl bromide (0.18 g, 1.5 mmol) was added to **2** (1.22 g, 0.5 mmol) and potassium carbonate (0.42 g, 3 mmol) in 20 mL of CH_3CN. The mixture was refluxed for 14 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.82 g (65%) of the title compound: IR (KBr) 2862 (m), 2162 (m), 1735 (s), 1654 (s), 1059 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.90−2.00 (m, 1H), 2.75−2.85 (m, 2H), 3.50−3.70 (s large, ≈180 H),

4.15−4.25 (m, 2H), 4.25−4.35 (m, 1H), 7.20−7.70 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 24.56, 61.88, 64.51, 64.93, 69.46, 70.51−71.08, 72.90, 81.36, 128.19, 128.59, 128.81, 129.01, 129.26, 129.31, 129.55, 130.60, 131.06, 132.96, 136.50, 139.95, 171.00, 172.57.

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene-amino))-4-pentynoate (6d). Propargyl bromide (0.06 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 3 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.475 g (97%) of the title compound: IR (KBr) 2868 (m), 2132 (m), 1736 (s), 1646 (m), 1142 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.95−2.00 (m, 1H), 2.75−2.90 (m, 2H), 3.50−3.80 (s large, ≈310H), 4.15−4.25 (m, 2H), 4.25−4.35 (m, 1H), 7.20−7.70 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 23.67, 62.02, 64.34, 64.76, 68.93, 69.28, 70.37−71.73, 72.95, 81.17, 128.42, 128.63, 128.84, 129.14, 129.36, 130.88, 136.32, 139.77, 170.79, 172.36; MS (Electrospray) *m*/*z*, n = 75, 1295.55 (+3), n = 80, 1015.78 (+4).

The same procedure as that for the synthesis of *N*-(diphenylmethylene amino)-pent-4-ynoic acid poly(ethylene glycol)-3400 ester **6d** was used in the same proportion, and the mixture was stirred at room temperature for 4 h to yield 0.43 g (88%) of the title compound.

Poly(ethylene glycol)-2000 Di(2(*N*-(diphenylmethylene-amino))-4-methylene-4-methoxycarbonylpentanoate) (5e). Methyl 2-(bromomethyl) acrylate (0.27 g, 1.5 mmol) was added to **2** (1.22 g, 0.5 mmol) and potassium carbonate (0.42 g, 3 mmol) in 20 mL of CH_3CN. The mixture was refluxed for 14 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.93 g (71%) of the title compound: IR (KBr) 2868 (m), 1726 (m), 1650 (s), 1633 (m), 1108 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.85 (dd, J_1 = 13.5 Hz, J_2 = 9 Hz, 1H), 3.07 (dd, J_1 = 13.5 Hz, $J_{2'}$ = 4 Hz, 1H), 3.50−3.70 (s large, ≈180H), 4.20−4.30 (m, 2H), 4.30−4.40 (m, 1H), 5.65 (s, 1H), 6.20 (s, 1H), 7.10−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 36.32, 52.05, 61.98, 64.25, 64.61, 69.36, 70.58−70.95, 72.98, 127.00, 128.43, 128.54, 128.69, 128.76, 129.01, 129.20, 129.35, 130.47, 130.81, 132.84, 136.72, 139.82, 167.23, 171.65, 171.83.

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene-amino))-4-methylene-4-methoxycarbonylpentanoate) (6e). Methyl 2-(bromomethyl) acrylate (0.07 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 3 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.44 g (88%) of the title compound: IR (KBr) 2869 (m), 1734 (m), 1646 (s), 1636 (m), 1095 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.85 (dd, J_1 = 13.5 Hz, J_2 = 9 Hz, 1H), 3.07 (dd, J_1 = 13.5 Hz, $J_{2'}$ = 4 Hz, 1H), 3.50−3.70 (s large, ≈310H), 4.20−4.30 (m, 2H), 4.30−4.40 (m, 1H), 5.65 (s, 1H), 6.20 (s, 1H), 7.10−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 29.99, 36.25, 51.96, 54.48, 64.17, 64.54, 69.28, 70.67−70.90, 126.90, 128.35, 128.46, 128.69, 128.75, 128.94, 129.11, 129.20, 130.73, 136.40, 136.68, 139.73, 167.10, 171.51, 171.69; MS (Electrospray) *m*/*z*, n = 75, 1335.06 (M + Na) (+3), n = 80, 1045.85 (+4).

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene-amino))-4-methylpentanoate) (6f). 1-Iodo-2-methylpropane (0.06 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 2 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.41 g (83%) of the title compound: IR (KBr) 2870 (m), 1772 (s), 1652 (m), 1276 (s), 1140 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.60−0.95 (m, 6H), 1.40−1.60 (m, 1H), 1.65−1.90 (m, 2H), 3.50−3.75 (s large, ≈310H), 4.05−4.15 (m, 1H), 4.15−4.30 (m, 2H), 7.15−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 22.07, 23.60, 25.02, 43.02, 62.02, 64.15, 64.32, 69.38, 70.38−71.72, 72.97, 116.85, 128.30, 128.39, 128.83, 129.08, 129.16, 130.64, 136.73, 139.96, 170.65, 173.04; MS (Electrospray) *m*/*z*, n = 75, 1300.54 (+3), n = 80, 1024.95 (+4).

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene amino))-4-phenylbutanoate) (6g). 2-Phenylethyl bromide (0.07 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 2 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.39 g (77%) of the title compound: IR (KBr) 2868 (m), 1736 (s), 1646 (m), 1354 (m), 1137 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.10−2.25 (m, 1H), 2.45−2.75 (m, 1H), 2.80−2.95 (m, 2H), 3.50−3.75 (s large, ≈310H), 4.10−4.25 (m, 1H), 4.25−4.35 (m, 2H), 7.15−7.90 (m, 15H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 32.43, 35.49, 61.72, 64.27, 65.01, 69.24, 70.52−71.58, 72.88, 87.34, 126.10, 128.03, 128.33, 128.58, 128.64, 128.81, 128.94, 129.06, 130.66, 136.51, 139.75, 141.72, 171.05, 172.24; MS (Electrospray) *m*/*z*, n = 75, 1339.32 (+3), n = 80, 1054.82 (+4).

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethylene-amino))-2-cyclohexylethanoate) (6h). Cyclohexyl iodide (0.08 g, 0.375 mmol) was added to poly(ethylene glycol)-3400 *N*-(diphenylmethylene) glycinate **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 8 h. After cooling, the base was filtered and the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.375 g (75%) of the title compound: IR (KBr) 2870 (m), 1738 (s), 1650 (m), 1366 (s), 1137 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.85−1.60 (m, 6H), 1.65−1.80 (m, 4H), 2.05−2.10 (m, 1H), 3.50−3.80 (s large, ≈310H), 4.15−4.25 (m, 1H), 4.25−4.35 (m, 2H), 7.10−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 26.53, 27.36, 29.11, 30.26, 42.19, 61.81, 64.02, 69.40, 70.49−71.33, 73.00, 128.37, 128.81, 128.91, 129.18, 130.60, 136.89, 140.02, 170.73, 172.28; MS (Electrospray) *m*/*z*, n = 75, 1325.53 (+3), n = 80, 1038.87 (+4).

Poly(ethylene glycol)-3400 Di(2(*N*-(diphenylmethyleneamino))-4-methoxycarbonylpentanoate) (6i). (−)-Methyl (*S*)-3-bromo-2-methylpropionate (0.07 g, 0.375 mmol) was added to **3** (0.48 g, 0.125 mmol) and cesium carbonate (0.24 g, 0.75 mmol) in 10 mL of CH_3CN. The mixture was refluxed for 6 h. After cooling, the base was filtered, the filtrate was concentrated, dissolved in CH_2Cl_2, filtered, and then precipitated in Et_2O. The product was filtered and dried in vacuo to yield 0.46 g (91%) of the title compound: IR (KBr) 2870 (m), 1734 (s), 1647 (m), 1276 (s), 1140 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.10 (dd, $J_1 = 28.5$ Hz, $J_2 =$ 7.0 Hz, 3H), 1.95−2.15 (m, 1H), 2.30−2.45 (m, 1H), 2.50−2.60 (m, 1H), 3.50−3.80 (s large, ≈310H), 4.05−4.15 (m, 1H), 4.20−4.30 (m, 2H), 7.15−7.50 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 17.57, 18.80, 36.40, 36.89, 37.38, 51.83, 51.93, 62.03, 63.64, 63.79, 64.51, 69.31, 70.68−71.73, 72.96, 128.29, 128.39, 128.75, 128.89, 129.08, 129.12, 129.19, 129.23, 130.78, 130.85, 136.44, 136.48, 139.61, 139.79, 171.47, 171.68, 172.02, 172.07, 176.69, 176.88; MS (Electrospray) *m*/*z*, $n = 75$, 1296.42 (+3), $n = 80$, 1027.97 (+4).

Cleavage of Poly(ethylene glycol)-3400. A solution of poly(ethylene glycol)-3400 supported alkylated Schiff base (1 equiv) and potassium cyanide (1.5 equiv) in 20 mL of MeOH was heated under reflux for 20 h. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and precipitated in ether. The poly(ethylene glycol) free was filtered, and the filtrate was washed three times with water and dried in vacuo to give the methyl ester derivative.

Methyl *N*-(Diphenylmethylene)glycinate (4). With **3** (0.96 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.094 g (74%) of the title compound: IR (KBr) 1748 (m), 1616 (s), 1184 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.75 (s, 3H), 4.20 (s, 2H), 7.15−7.70 (m, 10H); MS (Electrospray) $m/z = 254.22$ (M + 1).

Methyl 2(*N*-(Diphenylmethylene amino))hexanoate (4a). With **6a** (0.99 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.12 g (78%) of the title compound: IR (neat) 2854 (m), 1731 (s), 1626 (m), 1277 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, $J = 6.5$ Hz, 3H), 1.10−1.70 (m, 4H), 1.85−1.95 (m, 2H), 3.35−3.45 (m, 2H), 3;70 (s, 3H), 4.05−4;15 (m, 1H), 7;20−7.80 (m, 10H); MS (Electrospray) $m/z = 310.37$ (M + 1).

Methyl *N*-(Diphenylmethylene)phenylalaninate (4b). With **6b** (1.01 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.11 g (64%) of the title compound: IR (neat) 2869 (m), 1718 (s), 1676 (m), 1141 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.20−3.30 (m, 2H), 3.75 (s, 3H), 4.20−4.30 (dd, $J_1 = 9$ Hz, $J_2 = 4.5$ Hz, 1H), 7.10−7.70 (m, 15H); MS (Electrospray) $m/z = 344.24$ (M + 1).[20]

Methyl 2(*N*-(Diphenylmethyleneamino))-4-pentenoate (4c). (a) With **6c** (0.49 g, 0.125 mmol) and KCN (0.012 g, 0.1875 mmol) to yield 0.05 g (68%) of the title compound: IR (neat) 2922 (m), 1699 (s), 1599 (s), 1000 (s), 942 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.60−2.80 (m, 2H), 3.75 (s, 3H), 4.15−4.25 (m, 1H), 5.05−5.20 (m, 2H), 5.60−5.80 (m, 1H), 7.20−7.70 (m, 10H); MS (Electrospray) $m/z =$ 294.35 (M + 1).[21]

(b) With **6c** (0.49 g, 0.125 mmol) and NEt_3 (20% v/v in MeOH, 2 mL) in 8 mL of MeOH to yield 0.07 g (95%) of the title compound.

Methyl 2(*N*-(Diphenylmethyleneamino))-4-pentynoate (4d). With **6d** (0.98 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.11 g (76%) of the title compound: IR (neat) 2900 (m), 1740 (s), 1621 (m), 1212 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.00−2.10 (m, 1H), 2.80−2.95 (m, 2H), 3.70 (s, 3H), 4.30−4.45 (m, 1H), 7.20−7.70 (m, 10H); MS (Electrospray) $m/z = 292.33$ (M + 1).[22]

Methyl 2(*N*-(Diphenylmethyleneamino))-4-methylenepentane-1,5-dioate (4e). With **6e** (1.01 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.15 g (84%) of the title compound: IR (neat) 2923 (m), 1729 (s), 1660 (m), 1277 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.80 (dd, $J_1 =$ 13.5 Hz, $J_2 = 9$ Hz, 1H), 3.10 (dd, $J_1 = 13.5$ Hz, $J_{2'} = 4.5$ Hz, 1H), 3.55 (s, 3H), 3.75 (s, 3H), 4.35−4.45 (dd, $J_2 = 9$ Hz, $J_{2'} = 4.5$ Hz, 1H), 5.65 (s, 1H), 6.20 (s, 1H), 7.10−7,70 (m, 10H); MS (Electrospray) $m/z = 352.69$ (M + 1).

Methyl 2(*N*-(Diphenylmethyleneamino))leucinate (4f). With **6f** (1.23 g, 0.31 mmol) and KCN (0.030 g, 0.465 mmol) to yield 0.14 g (70%) of the title compound: IR (neat) 2959 (m), 1728 (m), 1660 (m), 1599 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.80−1.15 (m, 6H), 1.50−1.70 (m, 1H), 1.80−2.10 (m, 2H), 3.80 (s, 3H), 4.15−4.25 (m, 1H), 7.20−7.70 (m, 10H); MS (Electrospray) $m/z = 310.89$ (M + 1).

Methyl 2(*N*-(Diphenylmethyleneamino))-4-phenylbutanoate (4g). With **6g** (1.22 g, 0.30 mmol) and KCN (0.029 g, 0.45 mmol) to yield 0.17 g (79%) of the title compound: IR (neat) 2923 (m), 1731 (s), 1626 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.20−2.35 (m, 2H), 2.45−2.60 (m, 2H), 3.75 (s, 3H), 4.10−4.25 (m, 1H), 7.10−7.70 (m, 15H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 31.18, 34.33, 51.01, 63.88, 124.83, 126.75, 127.07, 127.25, 127.30, 127.35, 127.50, 127.64, 127.84, 135.27, 138.49, 140.40, 169.85, 171.74; MS (Electrospray) $m/z = 358.13$ (M + 1).

Methyl 2(*N*-(Diphenylmethylene amino))-2-cyclohexylethanoate (4h). With **6h** (1.002 g, 0.25 mmol) and KCN (0.024 g, 0.375 mmol) to yield 0.11 g (66%) of the title compound: IR (neat) 2923 (m), 1729 (s), 1626 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.85−1.65 (m, 6H), 1.65−1.90 (m, 4H), 2.05−2.25 (m, 1H), 3.75 (s, 3 H), 3.90 (d, $J = 6.5$ Hz, 1H), 7.20−7.80 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 25.12, 22.22, 27.83, 28.90, 41.01, 52.40, 64.84, 70.19, 126.97, 127.01, 127.26, 127.42, 127.53, 127.84, 135.52, 138.68, 171.61, 172.36; MS (Electrospray) $m/z = 336.40$ (M + 1).

Dimethyl 2(*N*-(Diphenylmethylene amino))-4-methylpentane-1,5-dioate (4i). With **6i** (1.69 g, 0.42 mmol) and KCN (0.041 g, 0.63 mmol) to yield 0.29 g (98%) of the title compound: IR (neat) 2920 (m), 1729 (s), 1660 (m), 1600 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.10 (dd, $J_1 = 28.5$ Hz, $J_2 = 7.0$ Hz, 3H), 1.95−2.10 (m, 1H), 2.25−2.40 (m, 1H), 2.45−2.60 (m, 1H), 3;50 (d, $J_2 = 7.0$ Hz, 3H), 3.70 (s, 3H), 4.10−4.20 (m, 1H), 7.15−7.50 (m, 10H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 17.57, 18.82, 36.27, 36.53, 36.93, 37.64, 37.65, 51.87, 52.00, 52.61, 52.97, 63.79, 63.88, 128.29, 128.47, 128.70, 128.96, 129.15, 129.19, 129.28, 129.32,

130.47, 130.86, 130.93, 132.83, 136.51, 136.54, 139.68, 139.85, 171.50; 171.75, 172.77, 172.81, 176.76, 176.94; MS (Electrospray) $m/z = 354.25$ (M + 1).

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