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Sequential Synthesis of (*E*)-α,*β*-Unsaturated Primary Amides with Complete Stereoselectivity†

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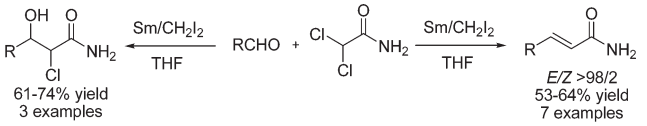


A novel, efficient, and totally stereoselective synthesis of (*E*)-α,*β*-unsaturated primary amides is reported. This process is consistent with a SmI_2-mediated sequential reaction of an unmasked samarium chloroacetamide enolate with an aldehyde, followed by a *β*-elimination to produce (*E*)-α,*β*-unsaturated primary amides in good yields.

Enolates derived from lithium, magnesium, and other classical metals are certainly useful reagents. The broad use of enolates in organic synthesis is a consequence of their ready preparation and ability to promote C−C bond-forming reactions with high selectivity and under mild conditions. As a major drawback, in some cases the applicability of enolates is limited by the basicity of these compounds. For this reason, reactions of metallic enolates with substrates containing functional groups with acidic hydrogens (unless protected) cannot be carried out. In the same way, lithium or magnesium enolates derived from primary amides are not available. Accordingly, if these species are required in synthesis transformations, two general strategies are followed: (i) carrying out reactions with protected amide enolates, followed by deprotection of the amide function, and (ii) alternatively, preparing dianionic species from primary amides. However, this later strategy finds prompt limitations associated with the low solubility of such species in organic solvents.[1]

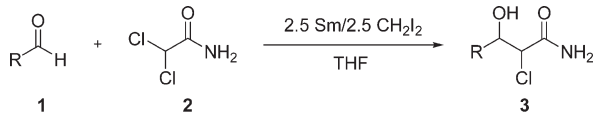
Previously, we have reported the preparation of acetic[2] and bromoacetic[3] acid derived samarium enolates by metalation of iodoacetic and dibromoacetic acids, respectively, with SmI_2.[4] The addition reaction of the acetic acid derived samarium enolate to aldehydes allowed accessing 3-hydroxy carboxylic acids in an efficient manner. Moreover, bromoacetic acid derived samarium enolates were used in the highly stereoselective preparation of (*E*)-α,*β*-unsaturated carboxylic acids through a sequential process involving an aldol-type reaction followed by an elimination step. Taking into account these precedents, generalization of this methodology to the preparation of Sm enolates derived from primary amides would undoubtedly be of interest.

In this paper we describe a new, easy, and efficient preparation of α,*β*-unsaturated primary amides through a sequential reaction involving a novel samarium enolate of a primary amide.

In early experiments, dichloroacetamide **2** was reacted with SmI_2 in the presence of the corresponding aldehyde **1**. In all cases 2-chloro-3-hydroxyamides **3** were obtained in moderate to high yields. The best results were obtained by generating SmI_2, *in situ* (from samarium powder and diiodomethane)[5] instead of using a previously generated samarium diiodide solution (Table 1). Accordingly, diiodomethane (2.5 equiv) was added dropwise to a suspension of the corresponding aldehyde **1** (1.0 equiv), dichloroacetamide **2** (1.0 equiv), and samarium powder (2.5 equiv) in 25 mL of dry THF at room temperature. The reaction mixtures were vigorously stirred for 3.5 h before they were hydrolyzed.

Compounds **3** were obtained as a mixture of diastereoisomers with diastereoisomeric ratios (dr) ranging from 1:1 to 1.4:1 as determined by ^1H NMR spectroscopy on the crude reaction products (Table 1).

TABLE 1. Synthesis of 2-Chloro-3-hydroxyamides 3



1 2 3

entry	3	R	dr	yield (%)
1	**3a**	n-C_7H_{15}	1.3:1	70
2	**3b**	*c*-Hex	1:1	74
3	**3c**	$PhCH_2CH_2$	1.4:1	61

† In Memoriam of Prof. José M. Concellón, who passed away on March 13, 2010.

(1) For reviews of dianions of carboxylic acids, see: (a) Petragnani, N.; Yonashiro, M. *Synthesis* **1982**, 521–578. (b) Thompson, C. M.; Green, D. L. C. *Tetrahedron* **1991**, *47*, 4223–4285.

(2) Concellón, J. M.; Concellón, C. *J. Org. Chem.* **2006**, *71*, 4428–4432.

(3) Concellón, J. M.; Concellón, C. *J. Org. Chem.* **2006**, *71*, 1728–1731.

(4) Reviews of synthetic applications of SmI_2: (a) Soderquist, J. A. *Aldrichimica Acta* **1991**, *24*, 15–23. (b) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29–68. (c) Molander, G. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 251−282. (d) Molander, G. A. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley: New York, 1994; pp 211−367. (e) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338. (f) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321–3354. (g) Krief, A.; Laval, A. M. *Chem. Rev.* **1999**, *99*, 745–777. (h) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727–2751. (i) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351–10372. (j) Concellón, J. M.; Rodríguez-Solla, H. *Chem. Soc. Rev.* **2004**, *33*, 599–609. (k) Jung, D. Y.; Kim, Y. H. *Synlett* **2005**, 3019–3032. (l) Concellón, J. M.; Rodríguez-Solla, H. *Eur. J. Org. Chem.* **2006**, 1613–1625. (m) Gopalaiah, K.; Kagan, H. B. *New J. Chem.* **2008**, *32*, 607–637. (n) Nicolaou, K. C.; Ellery, S. P.; Chen, J. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 7140–7165.

(5) For other reactions promoted by *in situ* generated SmI_2, see: Concellón, J. M.; Rodríguez-Solla, H.; Huerta, M.; Pérez-Andrés, J. A. *Eur. J. Org. Chem.* **2002**, 1839–1847.

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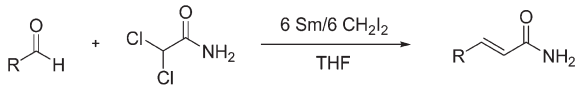
TABLE 2. Synthesis of (*E*)-α,β-Unsaturated Amides 4



1 2 4

entry	4	R	*E*/*Z*	yield (%)
1	**4a**	*n*-C_7H_{15}	>98/2	60
2	**4b**	*s*-Bu	>98/2	56
4	**4c**	*c*-Hex	>98/2	61
5	**4d**	$PhCH_2CH_2$	>98/2	53
6	**4e**	*t*-$BuCH_2CH(Me)CH_2$	>98/2	56
7	**4f**	(*Z*)-$EtCH{=}CH(CH_2)_5$	>98/2	64

As opposed to classical multistep reactions, sequential processes are synthetically advantageous because isolation of intermediates is not necessary. Considering our success in the preparation of compounds **3**, we contemplated the possibility of carrying out a one-pot sequential process from dichloroacetamide **2** directed toward the synthesis of unprotected α,β-unsaturated primary amides. In consequence, a mixture of aldehyde **1** (1.0 equiv), dichloroacetamide **2** (1.0 equiv), and samarium powder (6.0 equiv) in THF (25 mL) was treated with CH_2I_2 (6.0 equiv) and stirred for 12 h at room temperature. Rewardingly, (*E*)-α,β-unsaturated amides **4** were obtained, with total *E*-stereoselectivity and in good yields (Table 2). Byproducts generated from the hydrolysis of enolate intermediates by the amide acidic protons were not detected.

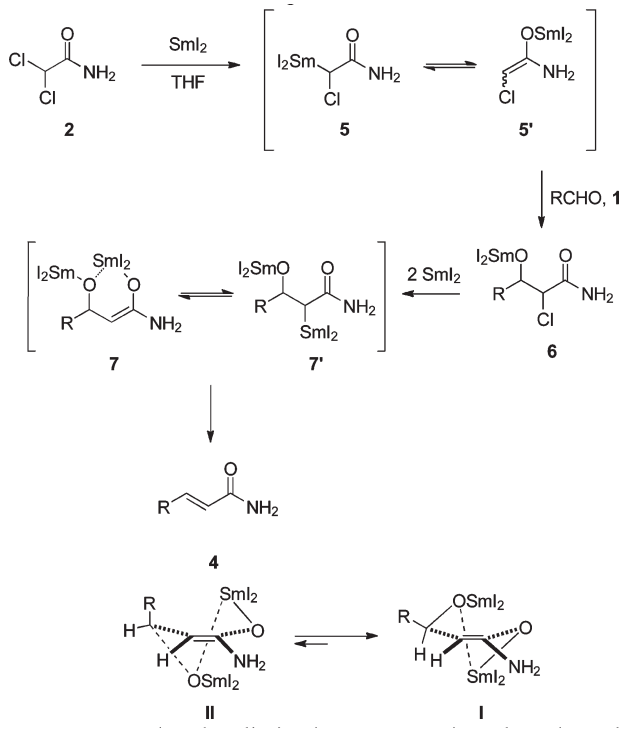
The total stereoselective outcome of the reaction was established on crude reaction mixtures by GC−MS analysis and ^{1}H NMR spectroscopy, revealing the presence of a single stereoisomer. The relative *E*-configuration of amides **4** was also assigned by ^{1}H NMR spectroscopy measuring the value of the coupling constants ($^3J_{H,H}$) for the olefinic protons.

α,β-Unsaturated amides **4** could be prepared from aliphatic (linear, branched or cyclic) aldehydes **1**. However, in our hands, aromatic amides (**4**, R = Ar) were never isolated.[6] To the best of our knowledge, this sequential C−C bond formation/elimination reaction constitutes the first example described in the literature in which primary α,β-unsaturated amides were obtained using unprotected amides as starting materials and avoiding protection/deprotection protocols.

To explain the observed results, we propose a mechanism similar to those previously considered for other SmI_2-promoted olefination reactions. In this way, dichloroacetamide **2** reacts with SmI_2 to generate the samarium enolate **5** (Scheme 1).[7] The addition reaction of **5** to aldehyde **1** affords the corresponding 2-chloro-3-oxy amide **6**. Metalation of **6** with an additional 2 equiv of samarium diiodide gives access to enolate intermediate **7**-**7′**, which would undergo a spontaneous elimination reaction, rendering after workup the corresponding α,β-unsaturated primary amide **4**.

The formation of the samarium enolate **5** (presenting two NH_2 acidic protons) could be explained on the basis of similar arguments used to justify the formation of acetic[2] and bromoacetic[3] acid derived samarium enolates. Therefore, we reckon that once dichloroacetamide **2** has reacted and the corresponding enolate is formed, the equilibrium **5** ↔ **5′** is fully displaced favoring the tautomeric form $ClCH{=}C(NH_2)$-$OSmI_2$ (**5′**) as a consequence of the high oxophilic character of Sm(III) ions (Scheme 1). This tautomer **5′** is capable of coexisting in the presence of a NH_2 group.

SCHEME 1. Mechanistic Proposal



2 5 5′ 7 7′ 6 4 II I

Further evidence reinforcing this argument is the preparation of β-hydroxy samarium enolates, previously obtained by treating the corresponding 2-chloro-3-hydroxyester[8] or amides[9] with SmI_2.

We assume that the elimination process takes place through a cyclic six-membered ring transition state **7**,[10] guided by coordination of the Sm^{III} center with the oxygen atom of the alcoholate function[11] (Scheme 2). Two conformations, **I** and **II**, are feasible for intermediate **7**. Conformer **I** is presumably more stable than **II**, as the R group adopts a *pseudo*-equatorial orientation, thus avoiding unfavorable interactions with the samarium coordination sphere. Elimination from **I** renders (*E*)-α,β-unsaturated amides **4**. Our group and others have previously proposed similar chairlike transition states to

(6) When aromatic aldehydes were employed as starting materials, products derived from their pinacol coupling were isolated instead of the corresponding α,β-unsaturated amides **4**.

(7) For recent revisions on Samarium-enolates, see: (a) Rudkin, I. M.; Miller, L. C.; Procter, D. J. *Organomet. Chem.* **2008**, *34*, 19–45. (b) Procter, D. J.; Flowers, R. A., II; Skrydstrup, T. *Organic Synthesis Using Samarium Diiodide: A Practical Guide*; RSC Publishing: Cambridge, 2010.

(8) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 2773–2775.

(9) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Chem.—Eur. J.* **2001**, *7*, 3062–3068.

(10) A similar model involving a chairlike transition state has been proposed to explain the selectivity observed in other reactions with SmI_2: (a) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453–463. (b) Urban, D.; Skrydstrup, T.; Beau, J. M. *J. Org. Chem.* **1998**, *63*, 2507–2516. (c) Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2002**, *124*, 6357–6381. (d) Enemrke, R. J.; Larsen, J.; Hjollund, G. H.; Skrydstrup, T.; Daasbjerg, K. *Organometallics* **2005**, *24*, 1252–1262. (e) Davis, T. A.; Chopade, P. R.; Hilmersson, G.; Flowers, R. A. *Org. Lett.* **2005**, *7*, 119–122.

(11) For a discussion of the highly oxophilic character of Sm(III) species, see: Molander, G. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon: Cambridge, 1991; Vol. 1, p 252.

explain the relative configuration of olefins obtained by other SmI_2-promoted elimination reactions.

In conclusion, we have demonstrated that the samarium enolate formed from dichloroacetamide can be easily prepared and employed in the synthesis of unmasked (*E*)-α,*β*-unsaturated primary amides. These compounds are obtained with complete *E*-stereoselectivity through a sequential two-step process: an aldol-type and a *β*-elimination reaction.

Experimental Section

Preparation of 2-Chloro-3-hydroxyamides (3). To a stirred suspension of aldehyde **1** (0.4 mmol), dichloroacetamide **2** (0.4 mmol), and samarium powder (1 mmol) in THF (10 mL) was added CH_2I_2 (1 mmol) dropwise at room temperature, and the mixture was stirred for 3.5 h. The excess of SmI_2 was removed by bubbling a stream of air through the solution. The crude reaction material was washed with 0.1 N (aq) HCl (10 mL) and was extracted with DCM (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography on silica gel (hexane/EtOAc 3:1) afforded pure chlorohydrines **3**.

2-Chloro-3-hydroxydecanamide (3a). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.69 (br s, 1 H), 6.60 (br s, 1 H), 6.22 (br s, 1 H), 6.13 (br s, 1 H), 4.35 (d, *J* = 2.3 Hz, 1 H), 4.26 (d, *J* = 5.7 Hz, 1 H), 4.20−4.16 (m, 1 H), 4.06−4.00 (m, 1 H), 3.30 (br s, 1 H), 2.81 (br s, 1 H), 1.67−1.46 (m, 4 H), 1.42−1.17 (m, 20 H), 0.86 (t, *J* = 6.3 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 171.0 (C), 170.7 (C), 72.8 (CH), 71.9 (CH), 63.6 (CH), 62.3 (CH), 33.6 (CH_2), 32.9 (CH_2), 31.7 (2 × CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (2 × CH_2), 25.5 (CH_2), 25.2 (CH_2), 22.5 (2 × CH_2), 14.0 (2 × CH_3); MS (70 eV, EI) *m*/*z* (%) 186 ([M^+ − Cl], 12), 122 (23), 95 (33), 93 (100), 55 (40); HRMS (70 eV) calcd for [$C_{10}H_{20}ClNO_2 - H_2O$] 203.1077, found 203.1086; IR (neat) 3383, 1663, 1081, 723 cm^{-1}; R_f = 0.30 (hexane/EtOAc 1:1).

2-Chloro-3-cyclohexyl-3-hydroxypropanamide (3b). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.66 (br 1 H), 6.64 (br 1 H), 5.34 (apparent s, 1 H), 5.08 (dd, *J* = 8.2, 6.7 Hz, 1 H), 1.91−0.90 (m, 11 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 164.7 (C), 78.5 (CH), 66.2 (CH), 42.1 (CH), 29.6 (CH_2), 27.8 (CH_2), 26.0 (CH_2), 25.5 (2×CH_2); MS (70 eV, EI) *m*/*z* (%) 187 ([M^+-H_2O], 15), 186 (100), 150 (79), 93 (15), 79 (20), 67 (10); HRMS (70 eV) calcd for [$C_9H_{16}ClNO_2 - H_2O$] 187.0734, found 187.0739; IR (neat) 3370, 1670, 1099, 740 cm^{-1}; R_f = 0.26 (hexane/EtOAc 3:1).

2-Chloro-3-hydroxy-5-phenylpentanamide (3c). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.30−7.20 (m, 7 H), 5.85 (apparent s, 1 H), 5.38−5.30 (m, 1 H), 3.56 (d, *J* = 3.8 Hz, 1 H), 2.90−2.70 (m, 2 H), 2.17−1.95 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 164.7 (C), 140.4 (C), 128.6 (2×CH), 128.4 (2×CH), 126.3 (CH), 74.8 (CH), 65.9 (CH), 36.3 (CH_2), 30.7 (CH_2); MS (70 eV, EI) *m*/*z* (%) 174 ([M^+ − Cl − H_2O], 2), 131 (100), 103 (27), 77 (10); HRMS (70 eV) calcd for [$C_{11}H_{14}ClNO_2$ − Cl − H_2O] 174.0919, found 174.0926; IR (neat) 3352, 1675, 1109, 766, cm^{-1}; R_f = 0.39 (hexane/EtOAc 3:1).

Synthesis of (*E*)-α,*β*-Unsaturated Amides (4). To a stirred suspension of aldehyde **1** (0.4 mmol), dichloroacetamide **2** (0.4 mmol), and samarium powder (2.4 mmol) in THF (25 mL) was added CH_2I_2 (2.4 mmol) dropwise at room temperature. After the mixture stirred vigorously for 12 h, the excess of SmI_2 was removed by bubbling a stream of air through the solution. The crude reaction material was washed with 0.1 N (aq) HCl (10 mL) and was extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Flash chromatography on silica gel (hexane/EtOAc 3:1) afforded pure (*E*)-α,*β*-unsaturated amides **4**.

(*E*)-2-Decenamide (4a). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.86 (dt, *J* = 15.2. 6.9 Hz,1 H), 5.82 (d, *J* = 15.2 Hz, 1 H), 5.43 (br s, 2 H), 2.22−2.15 (m, 2 H), 2.03−1.18 (m, 10 H), 0.78 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 168.1 (C), 146.6 (CH), 122.5 (CH), 32.0 (CH_2), 31.7 (CH_2), 29.0 (2×CH_2), 28.1 (CH_2), 22.5 (CH_2), 14.0 (CH_3); MS (70 eV, EI) *m*/*z* (%) 151 ([$M - H_2O]^+$, 1), 122 (40), 98 (91), 72 (89), 59 (100); HRMS (70 eV) calcd for [$C_{10}H_{19}NO$] 169.1467, found 169.1468; IR (neat) 3387, 1680, 1258 cm^{-1}; R_f = 0.25 (hexane/EtOAc 1:2).

(*E*)-4-Methyl-2-hexenamide (4b). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.74 (dd, *J* = 15.3, 7.7 Hz, 1 H), 5.78 (dd, *J* = 15.3, 3.0, Hz, 1 H), 5.60 (br s, 2 H), 2.22−2.17 (m, 1 H), 1.41−1.37 (m, 2 H), 1.03 (d, *J* = 6.5 Hz, 3 H), 0.87 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 168.2 (C), 151.6 (CH), 121.0 (CH), 37.9 (CH), 28.8 (CH_2), 19.0 (CH_3), 11.6 (CH_3); MS (ESI$^+$) *m*/*z* (%) 127 ([$M]^+$, 27), 112 (100), 98 (24), 83 (18), 70 (22), 57 (24); HRMS (ESI$^+$) calcd for [$C_7H_{14}NO]^+$ [M + H]$^+$ 128.1075, found 128.1070; IR (neat) 3406, 1676, 1458, 1266 cm^{-1}; R_f = 0.32 (EtOAc).

(*E*)-3-Cyclohexylacrilamide (4c). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.80 (dd, *J* = 15.5, 6.8 Hz, 1 H), 5.76 (d, *J* = 15.5 Hz, 1 H), 5.53 (br s, 2 H), 2.16−2.04 (m, 1 H), 1.97−1.65 (m, 5 H), 1.31−1.08 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 166.7 (C), 151.5 (CH), 120.1 (CH), 40.2 (CH), 31.8 (2×CH_2), 25.9 (CH_2), 25.7 (2×CH_2); MS (70 eV, EI) *m*/*z* (%) 153 ([$M]^+$, 100), 136 (50), 109 (35); HRMS (ESI$^+$) calcd for [$C_9H_{16}NO]^+$ [M + H]$^+$ 154.1231, found 154.1226; IR (neat) 3363, 1676, 1406 cm^{-1}; R_f = 0.50 (EtOAc).

(*E*)-5-Phenyl-2-pentenamide (4d). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.50−7.08 (m, 5 H), 6.91 (dt, *J* = 15.3, 6.9 Hz, 1 H), 5.85 (d, *J* = 15.3 Hz 1 H), 5.56 (br s, 2 H), 2.79 (t, *J* = 7.7 Hz, 2 H), 2.54 (c, *J* = 7.3 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 167.7 (C), 145.1 (CH), 140.8 (C), 128.5 (2xCH), 128.4 (2×CH), 126.1 (CH), 123.1 (CH); 34.4 (CH_2), 33.7 (CH_2); MS (70 eV, EI) *m*/*z* (%) 175 ([M]+, 2), 130 (9), 91 (100), 77 (3), 44 (5); HRMS (ESI$^+$) calcd for [$C_{11}H_{14}NO]^+$ [M + H]$^+$ 176.1075, found 176.1070; IR (neat) 3435, 1643, 1453, 1265 cm^{-1}; R_f = 0.35 (hexane/EtOAc 1:5).

(*E*)-5,7,7-Trimethyl-2-octenamide (4e). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.90−6.80 (m, 1 H), 5.84 (dt, *J* = 16.4, 1.5 Hz, 1 H), 5.54 (br s, 2 H), 2.16−2.14 (m, 1 H), 2.08−2.0 (m, 1 H), 1.98−1.64 (m, 2 H), 1.07 (dd, *J* = 14.0, 6.5 Hz, 1 H), 0.94 (d, *J* = 6.5 Hz, 3 H), 0.89 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 167.8 (C), 145.4 (CH), 123.7 (CH), 50.5 (CH_2), 41.8 (CH_2), 31.0 (C), 29.9 (3×CH_3), 29.0 (CH), 22.4 (CH_3); MS (ESI$^+$) *m*/*z* (%) 184 ([M+H]$^+$, 100), 142 (3), 128 (2), 102 (1); HRMS (ESI$^+$) calcd for [$C_{11}H_{22}NO]^+$ [M + H]$^+$ 184.1701, found 184.1696; IR (neat) 3055, 1686, 1422, 1264 cm^{-1}; R_f = 0.35 (hexane/EtOAc 1:2).

(2*E*,9*Z*)-Dodeca-2,9-dienamide (4f). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.85 (dt, *J* = 15.3, 6.9 Hz, 1 H), 5.81 (d, *J* = 15.3, 1 H), 5.58 (br s, 2 H), 5.40−5.25 (m, 2 H), 2.22−2.15 (m, 2 H), 2.07−1.96 (m, 4 H), 1.47−1.25 (m, 6 H), 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 167.9 (C), 146.4 (CH), 131.7 (CH), 128.9 (CH), 122.6 (CH), 31.9 (CH_2), 29.4 (CH_2); 28.7 (CH_2), 28.0 (CH_2), 26.8 (CH_2), 20.4 (CH_2), 14.3 (CH_3); MS (70 eV, EI) *m*/*z* (%) 195 ([$M]^+$, 100), 174 (9), 153 (5), 109 (15); HRMS (ESI$^+$) calcd for [$C_{12}H_{22}NO]^+$ [M + H]$^+$ 196.1701, found 196.1697; IR (neat) 3220, 1681, 1265, 1250 cm^{-1}; R_f = 0.80 (hexane/EtOAc 1:5).

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.