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Tetrahedron
Tetrahedron 62 (2006) 10193–10201

Synthesis of aminimides derived from oleic acid: a new family of drag-reducing surfactants

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Received 16 May 2006; revised 1 August 2006; accepted 4 August 2006
Available online 1 September 2006

Abstract—Large-scale syntheses of aminimide surfactants that serve as low temperature drag-reducing agents in ethylene glycol–water mixtures are described. Preliminary drag reduction results are presented and the susceptibility of the surfactants to methanolysis is discussed.

1. Introduction

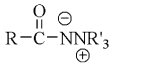
Addition of small amounts of materials to turbulent flow systems can reduce the pressure drop over a range of turbulent flow rates. This phenomenon is called drag reduction (DR).[1] Surfactant DR additives are of interest because they can be used to save pumping energy in district cooling systems wherein fluids are circulated through a closed loop (for example in buildings in large airports, urban districts, college campuses, and in hotel complexes). Such systems are widely used in the US and in Japan.

Surfactants constitute one family of DR additive.[2] These materials have the advantage over polymeric DR additives that they can recover from mechanical degradation by self-assembling into micelle structures responsible for DR.[3] Though cationic surfactants have been widely studied as DR additives and are effective, they are not easily biodegradable and could be an environmental hazard in case of a spill or leak into a stream, river or lake. Therefore, more easily biodegraded zwitterionic surfactants are of interest for use as drag-reducing additives. Aminimides derived from fatty acids (**1**) (Fig. 1) constitute a family of zwitterionic surfactants that have been used as detergents and adhesives, but never evaluated as DR additives.[4] We have examined the use of these materials as DR additives with some success in ethylene glycol (EG)–water. This article describes scaleable procedures for the preparation of these materials, presents preliminary results of DR studies in EG–water, and describes stability studies that reveal some new chemistry of aminimides.

2. Synthesis of aminimides

Aminimides derived from carboxylic acids have been prepared by two principle methods: (1) alkylation of the basic nitrogen of acylhydrazides[5] and (2) acylation of trialkylammonium amides with appropriate carboxylic acid derivatives.[6] The former method was used in what appears to be the first preparation of an aminimide surfactant[7] and the latter method has been used to prepare aminimides derived from fatty acids as long ago as 1972.[8] Our studies adopted the former method because it seemed to have the greatest flexibility for the preparation of a series of aminimides and it also seemed the most amenable to scale-up using simple laboratory equipment.

Scheme 1 outlines the preparation of seven aminimides based on a simple two-reaction sequence. Thus, treatment of commercially available oleoyl chloride (**2**) with slightly over 1 equiv of *N*,*N*-dimethylhydrazine in the presence of



1 R = fatty acid chain

Figure 1. Structure of aminimide surfactants.

Keywords: Aminimides; *N*-Acylhydrazides; District cooling; Drag reduction; Methanolysis.
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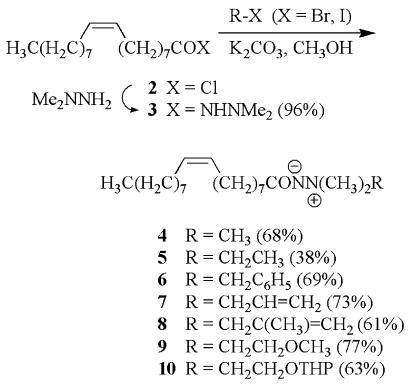
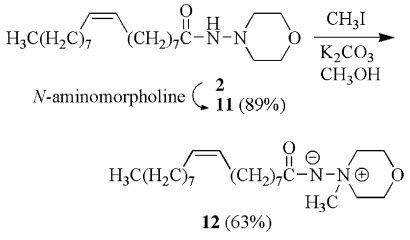
doi:10.1016/j.tet.2006.08.023



Scheme 1. Synthesis of aminimides **4**–**10**.

triethylamine provided *N*-acylhydrazide **3** in 96% yield after filtration through alumina to remove traces of amine salts. Treatment of **3** with a suitable alkyl halide in the presence of potassium carbonate using methanol as the solvent provided aminimides **4**–**10** in good yields after purification by chromatography over silica gel. Iodomethane was used for the synthesis of **4** while alkyl bromides were used for aminimides **5**–**10**. The yields are shown in parentheses in Scheme 1. These procedures were used to prepare multi-gram quantities of all aminimides shown in Scheme 1 (see Section 7). Scheme 2 describes the synthesis of an aminimide based on *N*-acylhydrazide **11**, prepared in 89% yield by reaction of oleoyl chloride with commercially available *N*-aminomorpholine. Alkylation of **11** with iodomethane provided aminimide **12** in 63% yield (Scheme 2).



Scheme 2. Synthesis of surfactant **12**.

Whereas the use of alkyl iodides and bromides provided materials that were pure enough for drag reduction studies, the aminimides derived from iodomethane (**4** and **12**) were usually more yellow in appearance than those derived from bromides. We suspected that this color was associated with iodine or traces of iodide that might be present in the products. Thus, for the synthesis of **4** we also examined dimethyl sulfate as the alkylating agent. This provided material that was less colored and did not become more yellow over time.

3. Characterization of *N*-acylhydrazides and aminimides

N-Acylhydrazides **3** and **11** exhibited isomerism characteristic of such compounds.[9] For example, the ^{1}H NMR spectrum of **3** exhibited two NH signals as broad singlets at δ 8.1 (minor isomer) and 8.7 (major isomer) in DMSO-d_6. In addition, two triplets were observed for the α-methylene ($CH_2C{=}O$) at δ 1.9 (major isomer) and 2.3 (minor isomer) and two singlets were observed for the $N(CH_3)_2$ groups at δ 2.41 (minor isomer) and 2.43 (major isomer). The ^{13}C NMR spectrum of **3** (DMSO-d_6) also showed two signals for the C=O groups at δ 174.3 and 169.4 and two signals for the $N(CH_3)_2$ groups at δ 47.7 and 46.2. The major and minor isomers appeared in a 62:38 ratio (based on integration of NH or $CH_2C{=}O$ signals in ^{1}H NMR spectrum). The major isomer was assigned *E*-geometry about the amide NC bond based on NOE experiments that established the proximal relationship between the NH and $CH_2C{=}O$ groups. The NMR spectra of **3** in $CDCl_3$ also showed the aforementioned geometrical isomerism. *N*-Acylhydrazide **11** exhibited similar spectroscopic behavior to **3**.

The spectroscopic behavior of aminimides **4**–**10** and **12** was more straightforward. All of these compounds exhibited the typical C=O stretch at approximately 1575 cm^{-1}.[4,10] Table 1 shows the average chemical shifts of seven ^{13}C NMR signals (C=O, C=C, NCH_3, allylic CH_2's, α-CH_2 relative to C=O, β-CH_2 relative to C=O, and terminal CH_3) and six ^{1}H NMR signals (CH=CH, NCH_3, $CH_2C{=}O$, $CH_2C{=}$, $CH_2CH_2C{=}O$, and terminal CH_3) observed for the eight aminimides prepared in this study. The assignments were based on chemical shift values and were supported by ^{1}H–^{13}C COSY experiments on aminimide **4** and selected DEPT experiments. These signals provide a signature for oleic acid derived aminimides. Appropriate signals unique to each aminimide, resulting from the different alkyl groups introduced in the *N*-acylhydrazide, were also observed in each case. Finally, the elemental composition of the aminimides was supported by HRMS (electrospray ionization).

All of the aforementioned aminimides were isolated as oils. A selection of these materials (**4**, **6**–**9**, **12**) exhibited hydrogen and nitrogen combustion analyses in accord with their elemental compositions. All of these compounds, however, gave combustion analyses that were slightly low in carbon. The IR spectra of all aminimides showed the presence of some water (approximately 3380 cm^{-1}). Karl Fischer titration indicated that the water content ranged from 1 to 6% by weight depending on the preparation. Spectral data, however, indicated that the materials prepared by the aforementioned procedures were pure enough for use in DR studies (see Supplementary data).

Table 1. Selected spectral data from aminimides

Spectrum	Observed	Signal
IR[a]	C=O stretch	1575
^{13}C NMR[b]	*C*=O	176.7
	*C*H=*C*H	129.7, 129.8
	N*C*H_3	53.7
	CH_2C=O	36.5
	CH_2CH=CH*C*H_2	27.10, 27.15
	CH_2CH_2C=O	26.7
	R–*C*H_3[c]	14.0
^{1}H NMR[b]	C*H*=C*H*	5.3
	NCH_3	3.3
	CH_2C=O	2.0
	CH_2CH=CHCH_2	1.95
	CH_2CH_2C=O	1.55
	R–CH_3[c]	0.8

[a] cm^{-1}.
[b] Parts per million from TMS in $CDCl_3$.
[c] From oleoyl group.

4. Drag reduction studies

4.1. Drag reduction measurement procedures

Drag reduction experiments were performed in a circulation flow system. The schematic is shown in Figure 2. The test section was a 2.18 m long stainless steel tube with a diameter of 10.9 mm. Two 4-gallon stainless steel surge tanks were installed to dampen pressure fluctuations in the loop. Other sections of the system were composed of all stainless steel parts and ½-inch tubing. Fluid temperatures at the inlet and outlet of the test section were measured by K-type thermocouples. A 2 kW heater, connected to a Variac, supplied the heat for high temperature runs. Pressure drops were measured by a Validyne differential pressure transducer. Flow rates were measured with a Rosemount Series 8700 magnetic flow meter. The system was equipped with a PolyScience chilling unit (Model KR-60A) to remove heat from the test system. The cooling temperature was controlled by a thermo-regulator (ranging from −30 to +30 °C, ±1%). The lowest temperature attainable in the test system was about −7 °C.

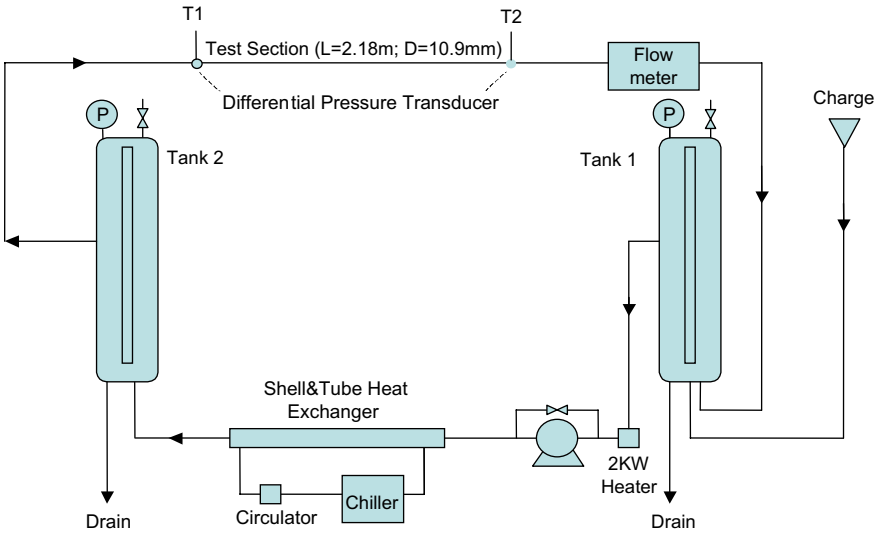


Figure 2. Schematic of drag reduction measurement flow loop.

Drag reduction in turbulent flow was determined from comparisons of measured pressure gradients ($\Delta P/L$) for the solution with additives and the pure solvent $(\Delta P/L)_S$ at the same flow rate. Drag reductions at different temperatures were calculated from the following equation over a Reynolds number range of 3×10^3–3×10^5:

$$\%\,\mathrm{DR} = \frac{(\Delta P/L)_S - (\Delta P/L)}{(\Delta P/L)_S} \times 100$$

4.2. Screening of surfactant DR candidates

Since approximately 30 g of surfactant was needed for drag reduction measurements in the recirculation system, screening of small surfactant samples were needed to focus on the most promising aminimides. For screening, approximately 60 mL of surfactant solution was stirred in a beaker by a magnetic stirrer. After the stirrer is stopped, the solution slows down in the direction of the swirling motion. Then, if it is viscoelastic, it will swirl in the opposite direction. The shorter the time between stopping the stirrer and the start of the back-swirl (swirl decay time), the greater the viscoelasticity. Although some non-viscoelastic surfactant systems have been observed with DR effectiveness, most surfactant DR additives are viscoelastic and have a distinct swirl decay time. To the best of our knowledge, a non-drag reducing but viscoelastic surfactant system in its dilute regime has never been reported. Therefore, this method was applied to screen small samples of the synthesized surfactants to select the most promising ones for preparing larger samples for drag reduction measurements.

4.3. Drag reduction results

On the basis of the aforementioned swirl test, and with the objective of testing a variety of structural types, aminimides **4**, **9**, and **12** were selected for evaluation as DR additives. These studies were conducted in the circulation flow system described in Section 4.1 over a Reynolds number range of 3×10^3–3×10^5 in 20% ethylene glycol–80% water. The behavior of DR additives in 20% EG–water is of special interest because its useful operating temperature range in district cooling systems (−5 to +15 °C) is twice the temperature range available in water (+5 to +15 °C), thus reducing the mass flow requirements by about half.

Table 2 documents the maximum % drag reduction at two temperatures in 20% EG–water. The aminimide surfactants clearly behave as good DR additives over a potentially useful range of temperatures in district cooling systems. The apparatus used to obtain the results shown in Table 2 holds a volume of about 30 L of fluid. Evaluation of aminimide **4** in a 1000-L system indicates that it remains a good DR additive

Table 2. Drag reduction of aminimide surfactants in 20% ethylene glycol–80% water at selected temperatures

[Surfactant]	Temperature (°C)	Max % drag reduction
[**4**]=6 mM	20	80
[**4**]=6 mM	−5	64
[**9**]=6 mM	20	72
[**9**]=6 mM	−1	67
[**12**]=6 mM	20	81
[**12**]=6 mM	−5	83

at even lower concentrations (% DR at 25 and −5 °C=59 and 47%, respectively, at 50 ppm).[11] Finally, cryo-TEM evaluation of 20% EG–water solutions of **4** indicated the presence of thread-like micelles at −5 °C.[12] It is generally believed that such micelles are an indication that a given surfactant will behave as an effective DR additive. Additional details of DR studies of these aminimides are reported elsewhere.[13]

4.4. Comparisons with commercial zwitterionics

DR results of three commercial zwitterionic surfactants in 20% ethylene glycol–80% water solvents are shown in Table 3 for comparison with the results in Table 2.[14] DR0206 (Akzo Nobel) has 20% myristylamidopropylbetaine, 10% rapeseedamidopropylbetaine, and 5% sodium alkylbenzenesulfonate (C_{10}–C_{13}). It was not DR effective in 20% EG–water alone but showed DR above 50% with the addition of 145 mM $NaNO_2$. Chemoxide OL (Chemron) is largely *N*,*N*-dimethyloleoylamine oxide. No DR effectiveness was observed for 5 mM (~2000 ppm) solutions of Chemoxide OL in 20% EG–water unless $NaNO_2$ was added. Results with 5 mM Chemoxide OL+10 mM $NaNO_2$ are shown in Table 3. Chembetaine OL (Chemron) is composed of oleyl betaine and was used with the addition of sodium dodecylbenzenesulfonate (SDBS) as a DR additive. The results of 4.8 mM Chembetaine OL+1.2 mM SDBS+6 mM $NaNO_2$ are also shown in Table 3. Thus, the aminimides evaluated in Table 2 compare very favorably with several commercially available surfactants used as DR additives.

Table 3. Drag reduction of selected commercial zwitterionic surfactant systems in 20% ethylene glycol–80% water at selected temperatures

Surfactant	Temperature (°C)	Max % drag reduction
DR0206 (9 mM)–$NaNO_2$ (145 mM)	15	45
DR0206 (9 mM)–$NaNO_2$ (145 mM)	2	52
Chemoxide OL (5 mM)–$NaNO_2$ (10 mM)	20	69
Chemoxide OL (5 mM)–$NaNO_2$ (10 mM)	5	57
Chembetaine OL (4.8 mM)–SDBS (1.2 mM)–$NaNO_2$ (6 mM)	20	0
Chembetaine OL (4.8 mM)–SDBS (1.2 mM)–$NaNO_2$ (6 mM)	−4	8

5. Stability studies

District cooling systems normally operate at basic pH's to minimize corrosion in the pipes. Nonetheless, the stability of aminimide surfactants under DR conditions was a matter of concern. This concern was in part prompted by the

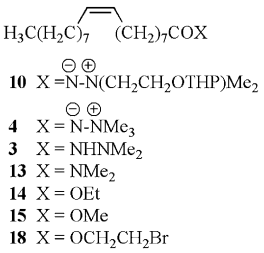
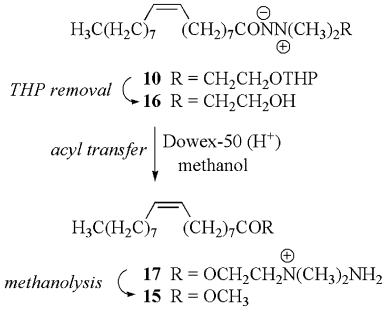


Figure 3. Selected oleic acid derivatives.

observation that attempts to remove the tetrahydropyranyl acetal group of **10** using methanol and Dowex-50 (H^+) at room temperature for 6.25 h led to methanolysis of the aminimide with formation of methyl oleate (**15**) in 66% yield (Fig. 3). These concerns were eliminated when it was shown that aminimide **4** could be recovered unchanged from a 20% EG–water solution that had been used in DR studies and stored for periods up to one month. Nonetheless, the behavior of **10** led us to evaluate the stability of aminimide **4**, and other oleic acid derivatives, under the aforementioned methanolysis conditions. In contrast to **10**, aminimide **4** did not undergo methanolysis under the aforementioned conditions. Instead, it was adsorbed on the Dowex-50 resin, presumably by protonation of the acylated nitrogen to form an ionic complex.[15] Warming the mixture at 70 °C, however, resulted in gradual production of methyl oleate (**15**) and after 24 h **15** could be isolated in 70% yield. For the purpose of comparison, acylhydrazine **3**, *N*,*N*-dimethyloleamide (**13**), and ethyl oleate (**14**) were also treated with Dowex-50 in methanol at 70 °C for 24 h. Whereas acylhydrazide **3** gave a 94% yield of methyl oleate under these conditions, amide **13** was recovered unchanged and ethyl oleate (**14**) was converted to a 62:38 mixture of the methyl and ethyl esters **15** and **14**, respectively. Therefore, under the acidic conditions described above, the relative rates of methanolysis of a series of carboxylic acid derivatives qualitatively appear to be amides<<<esters<aminimides~*N*-acylhydrazides.

The facile methanolysis of aminimide **10** can be explained (in part) by neighboring group participation (Scheme 3). Initial methanolysis of the THP ether would afford **16**. Intramolecular acyl transfer from nitrogen to oxygen would provide ester **17** and methanolysis of **17** would then provide the observed product **15**.



Scheme 3. Methanolysis of aminimide **10**.

Supporting evidence for this supposition follows. On one occasion it was found that treatment of **10** with $CuCl_2$

dihydrate in methanol at reflux for several hours provided a compound whose spectral data were consistent with those of ester **17** (or its conjugate base). Critical ^{1}H and ^{13}C NMR chemical shifts of **17** were consistent with those observed for methyl oleate (**15**) and not with those observed for aminimides. For example, the α-$CH_2C{=}O$ signal appears at δ 2.4 in the ^{1}H NMR spectrum of the presumed **17**. This signal appears at δ 2.35 in esters **14** and **15**, and at δ 2.0 for typical aminimides. The Cu(II)-mediated methanolysis, however, was difficult to reproduce. Therefore, an independent synthesis of **17** was undertaken to confirm the structure assignment and to see if **17** was kinetically competent to be an intermediate in the Dowex-50 mediated conversion of **10** to **15**. Treatment of oleoyl chloride (**2**) with 2-bromoethanol provided ester **18** (Fig. 3) in 94% yield. Reaction of **18** with *N*,*N*-dimethylhydrazine in tetrahydrofuran gave **17** (97%) with ^{1}H and ^{13}C NMR spectra identical to the material obtained from the Cu(II)-mediated methanolysis experiment.[16] In addition, the structure assignment of **17** was supported by the presence of ester (1740 cm^{-1}) and amine (3150 and 3210 cm^{-1}) stretching frequencies in its IR spectrum. Finally, when **17** was subjected to the methanolysis conditions used with aminimide **10** (methanol, Dowex-50, room temperature, 6.25 h), methyl oleate (**15**) was obtained in 77% yield. These experiments support the mechanistic hypothesis set forth in Scheme 3. The ease with which aminimides **4** and **10** and ester **17** undergo methanolysis is notable. A comparison of their rates of hydrolysis with a variety of acylating agents, including choline derivatives, will be reported in due course.[17]

6. Summary

This article describes the large-scale synthesis of aminimide surfactants that show promise as DR additives in 20% ethylene glycol–80% water. Procedures have been reported that are amenable to the synthesis of the quantities of material needed for large-scale DR experiments.[18] Stability studies reveal that standard aminimide surfactants are slightly more susceptible to methanolysis than esters under one set of acidic conditions. It has also been shown that one *N*-hydroxyethyl substituted aminimide undergoes methanolysis at faster rate than standard aminimides due (in part) to neighboring group participation.

7. Experimental

7.1. General experimental procedures

Solvents were purchased from commercial sources and used without purification. All reagents were purchased from commercial sources and not purified prior to use unless stated otherwise. Dowex-50WX8-100 was purchased from Aldrich Chemical Company and was used without purification or acid/base washing. Chromatography was conducted over silica gel. NMR spectra are reported in δ units from external tetramethylsilane. Copies of all spectra, including ^{13}C expansions, DEPT, and NOE experiments, are provided as Supplementary data. Combustion analytical data are reported as Supplementary data (for **4**, **6–9**, and **12**) along with adjustments for the presence of water, determined by Karl Fischer titration.[19]

7.1.1. *N*-Acylhydrazide 3. A three-neck flask equipped with a mechanical stirrer was charged with 220 g (0.73 mol) of freshly distilled oleoyl chloride in 1.0 L of toluene. The flask was cooled to 5 °C using an ice water bath and 68 mL (52.6 g, 0.88 mol) of 1,1-dimethylhydrazine was carefully added using a pressure equalizing addition funnel. The reaction was stirred for an additional 5 min and 123 mL (88.5 g, 0.88 mol) of triethylamine was added. The cold bath was removed and the reaction was stirred at room temperature for 24 h. The resulting heterogeneous mixture was filtered and the precipitate was rinsed with 200 mL of benzene. The combined filtrates were concentrated in vacuo to afford 234 g (97%) of crude **3** as a yellow liquid suitable for use in the next reaction. On one occasion when the reaction was performed on a 0.37 mol scale, the crude product was purified by chromatography over 800 g of neutral alumina (eluted with 1:1 ethyl acetate–hexanes) to give 114 g (96%) of acylhydrazide **3** as a pale yellow liquid: IR (neat) 3194, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.5–1.7 (m, 2H, CH_2CH_2CO), 1.8–2.1 (m, 4H, $H_2CC{=}$), 2.3–2.6 (m, 8H, CH_3N, CH_2CO), 5.2–5.4 (m, 2H, CH=CH), 6.1–6.2 (1H, NH, isomer 1), 6.2–6.3 (1H, NH, isomer 2); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.0, 22.6, 24.8, 27.1, 29.06, 29.11, 29.15, 29.25, 29.39, 29.45, 29.63, 29.7, 31.84, 31.92, 47.5, 48.6, 129.6, 129.8, 171.0 (isomer 1), 176.0 (isomer 2); HRMS (ESI) calcd for $C_{20}H_{40}N_2O+H^+$: *m*/*z* 325.3219, found: *m*/*z* 325.3216.

7.1.2. Aminimide 4. To a one-neck round bottom flask equipped with a football shaped stir bar and a condenser fitted with a calcium chloride drying tube were added 132.9 g (0.41 mol) of *N*-acylhydrazide **3**, 300 mL of methanol, 135.8 g (0.98 mol) of potassium carbonate, and 76.6 mL (174.7 g, 1.23 mol) of methyl iodide. The mixture was warmed under reflux for 24 h, cooled to room temperature, and 300 mL of dichloromethane was added. The solution was filtered and the filtrate was concentrated in vacuo. The crude product was chromatographed over 600 g of silica gel (eluted with ethyl acetate followed by 1:1 ethyl acetate–methanol) to give 94 g (68%) of the aminimide **4** as a pale yellow oil: IR (CCl_4) 1577 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 20H), 1.4–1.6 (m, 2H, CH_2CH_2CO), 1.8–2.0 (m, 6H, CH_2CO, $CH_2CH{=}$), 3.3 (s, 9H, CH_3N), 5.2–5.3 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (q), 22.6 (t), 26.7 (t, C_β), 27.15 (t, C8 or C11), 27.18 (t, C11 or C8), 29.40 (t), 29.46 (t), 29.49 (t), 29.72 (t), 31.8 (t), 36.6 (t, C_α), 55.4 (q, NMe), 129.80 (d), 129.85 (d), 177.0 (s) (four aliphatic carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{21}H_{40}N_2ONa$: *m*/*z* 361.3189, found: *m*/*z* 361.3200.

7.1.3. Aminimide 5. A mixture of 15.0 g (46.3 mmol) of *N*-acylhydrazide **3**, 50 mL of methanol, 15.3 g (0.11 mol) of potassium carbonate, and 28.0 mL (41.8 g, 0.37 mol) of ethyl bromide was warmed at 70 °C for 48 h, cooled to room temperature, and 60 mL of dichloromethane was added. The solution was filtered and the filtrate was concentrated in vacuo. The crude product was purified by chromatography over 150 g of silica gel (eluted with ethyl acetate followed by 9:1 ethyl acetate–methanol) to give 6.1 g (38%) of the aminimide **5** as a colorless oil: IR (CCl_4) 1578 cm^{-1}; ^{1}H NMR

($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 21H), 1.5 (m, 2H, CH_2CH$_2$CO), 1.95 (m, 4H, CH_2C=), 2.0 (t, J=7 Hz, 2H, CH_2CO), 3.3 (s, 6H, CH_3N), 3.7 (q, J=7.5 Hz, 2H, CH_2N), 5.2–5.3 (m, 2H, CH=); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.9, 13.9, 22.5, 26.7, 26.99, 27.02, 29.1, 29.25, 29.30, 29.40, 29.56, 29.58, 31.7, 36.3, 52.8 (NCH_3), 60.3, 129.62, 129.70, 176.4 (two carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{22}H_{42}N_2O$+H$^+$: m/z 353.3532, found: m/z 353.3521.

7.1.4. Aminimide 6. A mixture of 15.0 g (46.3 mmol) of *N*-acylhydrazide **3**, 50 mL of methanol, 15.3 g (0.11 mol) of potassium carbonate, and 13.8 mL (19.8 g, 115.8 mmol) of benzyl bromide was warmed overnight at 60 °C for 48 h, cooled to room temperature, and 60 mL of dichloromethane was added. The solution was filtered and the filtrate was concentrated in vacuo. The crude product was chromatographed over 150 g of silica gel (eluted with ethyl acetate followed by 9:1 ethyl acetate–hexanes) to give 10.5 g (55%) of the aminimide **6** as a colorless oil: IR (CCl_4) 1573 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 20H), 1.4–1.6 (m, 2H, CH_2CH$_2$CO), 1.95 (m, 6H, CH_2CO, CH_2C=), 3.3 (s, 6H, CH_3N), 4.9 (s, 2H, CH_2N), 5.2–5.3 (m, 2H, CH=CH), 7.3–7.5 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 22.6, 26.7, 27.18, 27.21, 29.27, 29.45, 29.48, 29.6, 29.75, 29.77, 31.9, 36.8, 52.8 (NCH_3), 67.7 (NCH_2), 128.74, 129.8, 129.9, 132.4, 176.9 (two aromatic and two aliphatic carbons were not observed due to overlap of signals); HRMS (ESI) calcd for $C_{27}H_{46}N_2ONa$: m/z 437.3508, found: m/z 437.3513.

7.1.5. Aminimide 7. A mixture of 15.0 g (46.3 mmol) of *N*-acylhydrazide **3**, 50 mL of methanol, 15.3 g (0.18 mol) of potassium carbonate, and 7.8 mL (11.2 g, 92.6 mol) of allyl bromide was warmed at 60 °C for 24 h, cooled to room temperature, and 60 mL of dichloromethane was added. The solution was filtered and the filtrate was concentrated in vacuo. The crude product was chromatographed over 150 g of silica gel (eluted with ethyl acetate followed by 20:1 ethyl acetate–methanol) to give 11.6 g (69%) of the aminimide **7** as a colorless oil: IR (CCl_4) 1576 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 20H), 1.5 (m, 2H, CH_2CH$_2$CO), 1.95 (m, 6H, CH_2CO and CH_2C=), 3.2 (s, 6H, CH_3N), 4.3 (d, J=7.5 Hz, 2H, CH_2N), 5.2–5.3 (m, 2H, CH=CH), 5.4–5.5 (m, 2H, =CH_2), 5.9–6.1 (m, 1H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 22.5, 26.6, 27.02, 27.05, 29.1, 29.27, 29.33, 29.42, 29.59, 29.61, 31.7, 36.4, 52.8 (NCH_3), 67.3 (NCH_2), 125.0, 127.4, 129.65, 129.73, 176.6 (two aliphatic carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{23}H_{44}N_2ONa$: m/z 365.3532, found: m/z 365.3532.

7.1.6. Aminimide 8. A mixture of 10.0 g (30.9 mmol) of *N*-acylhydrazide **3**, 40 mL of methanol, 10.3 g (74.2 mmol) of potassium carbonate, and 14.1 mL (18.7 g, 139.1 mol) of 3-bromo-2-methylpropene was warmed at 70 °C for 48 h, cooled to room temperature, and 60 mL of dichloromethane was added. The solution was filtered and the filtrate was concentrated in vacuo. The crude product was chromatographed over 120 g of silica gel (eluted with ethyl acetate followed by 7:3 ethyl acetate–methanol) to give 8.5 g (73%) of the aminimide **8** as a colorless oil: IR (CCl_4) 1576 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 20H), 1.55 (m, 2H, CH_2CH$_2$CO), 1.9–2.0 (m, 9H, CH_3C=, CH_2C=O, CH_2C=), 3.3 (s, 6H, CH_3N), 4.4 (s, 2H, CH_2N), 5.1 (s, 2H, =CH_2), 5.2–5.3 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.8 (q), 22.4 (t), 22.8 (q), 26.3 (t), 26.90 (t), 26.93 (t), 29.01 (t), 29.16 (t), 29.22 (t), 29.38 (t), 29.48 (t), 29.50 (t), 31.6 (t), 36.5 (t), 53.4 (q, NCH_3), 69.4 (t, NCH_2), 123.3 (t), 129.5 (d), 129.6 (d), 136.6 (s), 176.5 (s) (two aliphatic carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{24}H_{46}N_2ONa$: m/z 401.3508, found: m/z 401.3513.

7.1.7. Aminimide 9. To a one-neck round bottom flask equipped with a football shaped stir bar and a condenser fitted with a calcium chloride drying tube were added 70 g (0.22 mol) of the *N*-acylhydrazide **3**, 200 mL of absolute ethanol, 72.8 g (0.53 mol) of potassium carbonate, and 61.2 g (0.44 mol) of 2-bromoethyl methyl ether. The mixture was warmed under reflux for four days, cooled to room temperature, 200 mL of dichloromethane was added, and the heterogeneous mixture was filtered. The filtrate was concentrated in vacuo and the crude product was purified by chromatography over 300 g of silica gel (eluted with ethyl acetate followed by 4:1 ethyl acetate–methanol) to give 51.5 g (61%) of the aminimide **9** as a pale yellow oil: IR (CCl_4) 1573 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.5 (quintet, J=7 Hz, 2H, CH_2CH$_2$CO), 1.9–2.1 (m, 6H, CH_2CO, CH_2C=), 3.20–3.23 (two s, 9H, CH_3O, CH_3N), 3.6–3.7 (m, 2H), 3.9–4.0 (m, 2H), 5.27 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 22.6, 26.7, 27.1, 27.18, 29.24, 29.38, 29.44, 29.53, 29.7, 29.74, 31.8, 36.4, 55.0, 58.7, 64.1, 67.0, 129.77, 129.83, 176.6 (two aliphatic carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{23}H_{46}N_2O_2Na$: m/z 405.3424, found: m/z 405.3451.

7.1.8. Aminimide 10. To a one-neck round bottom flask equipped with a football shaped stir bar and a condenser fitted with a calcium chloride drying tube were added 6.8 g (0.021 mol) *N*-acylhydrazide **3**, 150 mL of absolute ethanol, 6.9 g (0.05 mol) of potassium carbonate, and 9.1 g (44 mmol) of the tetrahydropyranyl ether of 2-bromoethanol.[20] The mixture was warmed under reflux for five days, cooled to room temperature, 80 mL of dichloromethane was added, and the mixture was filtered. The filtrate was concentrated in vacuo and the crude product was purified by chromatography over 120 g of silica (eluted with ethyl acetate followed by 4:1 ethyl acetate–methanol) to afford 7 g (77%) of the aminimide **10** as a pale yellow oil: IR (CCl_4) 1574 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.4–1.6 (m, 6H), 1.6–1.8 (m, 2H), 1.8–2.0 (m, 6H), 3.30 and 3.35 (two s, 6H, CH_3N), 3.45 (m, 1H), 3.75 (m, 2H), 3.85 (m, 1H), 4.0 (m, 2H), 4.55 (m, 1H, OCHO), 5.3 (m, 2H, CH=); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 19.5, 22.5, 25.1, 26.8, 27.09, 27.13, 29.19, 29.35, 29.39, 29.53, 29.66, 29.69, 30.4, 31.8, 36.5, 54.5, 54.9, 62.11, 62.7, 64.2, 99.2, 129.7, 129.8, 176.7 (one aliphatic carbon was not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{27}H_{52}N_2O_2$+H$^+$: m/z 453.4056, found: m/z 452.4048.

7.1.9. *N*-Acylhydrazide 11. A one-neck round bottom flask equipped with a football shaped stir bar and an addition funnel was charged with 25 g (0.24 mol) of *N*-aminomorpholine and 350 mL of benzene. The addition funnel was charged with 80 g (0.22 mol) of oleoyl chloride (85% solution) and the acid chloride was added dropwise to the hydrazine at 5 °C over a period of 25 min. Upon completion of the addition, 150 mL of benzene was added, the cold bath was removed, and the heterogeneous reaction mixture was stirred for 24 h at room temperature. The resulting mixture was filtered and the filter cake was rinsed with 80 mL of benzene. The combined filtrates were concentrated in vacuo to afford 71.4 g (89%) of acylhydrazide **11** as a yellow solid, suitable for use in subsequent reactions without further purification: mp 87–88 °C; IR (neat) 3250, 3196, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.3 (m, 20H), 1.4–1.6 (m, 2H, CH_2CH_2CO), 1.8–2.0 (m, 5H), 2.3 (t, J=7.5 Hz, 1H), 2.4–2.9 (m, 4H), 3.4–3.8 (m, 4H), 5.2–5.3 (m, 2H), 7.0–7.1 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, diagnostic signals) δ 55.4 and 56.6 (CH_2N of geometrical isomers), 66.1 and 66.2 (CH_2O of geometrical isomers), 170.4 and 176.4 (C=O of geometrical isomers); HRMS (ESI) calcd for $C_{22}H_{42}N_2O_2Na$: m/z 389.3144, found: m/z 389.3139.

7.1.10. Aminimide 12. To a one-neck round bottom flask equipped with a football shaped stir bar and a condenser fitted with a calcium chloride drying tube were added 35.5 g (97 mmol) of *N*-acylhydrazide **11**, 120 mL of methanol, 32 g (23 mmol) of potassium carbonate, and 41.3 g (29 mmol) of methyl iodide. The mixture was warmed under reflux for 24 h, cooled to room temperature, 100 mL of dichloromethane was added, and the mixture was filtered. The filtrate was concentrated in vacuo and the residual crude product was purified by chromatography over 250 g of silica gel (eluted with ethyl acetate followed by methanol) to give 23 g (63%) of the aminimide **12** as a yellow semi-solid: IR (CCl_4) 1577 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.5 (quintet, J=7 Hz, 2H, CH_2CH_2CO), 1.9–2.0 (m, 4H, CH_2C=), 2.1 (t, J=7 Hz, 2H, CH_2CO), 3.1 (td, J=7, 1.2 Hz, 2H), 3.4 (s, 3H, CH_3N), 3.7 (d, J=12 Hz, 2H), 4.2 (t, J=12 Hz, 2H), 4.3 (d, J=12 Hz, 2H), 5.23 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 22.6, 26.8, 27.19, 27.2, 29.3, 29.4, 29.5, 29.60, 29.67, 29.75, 29.77, 31.8, 36.9, 53.4 (NCH_3), 61.6, 62.2, 129.85, 129.86, 176.9 (one carbon was not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{23}H_{44}N_2O_2Na$: m/z 403.3281, found: m/z 403.3294.

7.1.11. Methanolysis of aminimide 10. A mixture of 200 mg (0.44 mmol) of aminimide **10**, 10 mL of methanol, and 400 mg of acidic Dowex-50WX8-100 was stirred at room temperature for 12 h. The mixture was filtered and the filtrate was concentrated in vacuo to afford 120 mg (92% yield) of pure methyl oleate (**15**): ^1H NMR ($CDCl_3$, 400 MHz) δ 0.8 (t, J=7.5 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.6 (quintet, J=7 Hz, 2H, CH_2CH_2CO), 2.0 (m, 4H, CH_2C=), 2.3 (t, J=7 Hz, 2H, CH_2CO), 3.6 (s, 3H, CH_3O), 5.3 (m, 2H, CH=CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (q), 22.7 (t), 24.9 (t), 27.1 (t), 27.2 (t), 29.07 (t), 29.11 (t), 29.13 (t), 29.3 (t), 29.5 (t), 29.67 (t), 29.75 (t), 31.9 (t), 34.1 (t), 51.4 (q), 129.7 (d), 129.9 (d), 174.2 (s) (the signal at δ 29.3 represents two carbons based on intensity).

7.1.12. Methanolysis of *N*-acylhydrazide 3. A mixture of 200 mg (0.61 mmol) of *N*-acylhydrazide **3**, 10 mL of methanol, and 400 mg of acidic Dowex-50WX8-100 was stirred at 70 °C (oil bath temperature) for 24 h. The mixture was filtered and the filtrate was concentrated in vacuo to afford 170 mg (94%) of methyl oleate (**15**).

7.1.13. Methanolysis of aminimide 4. A mixture of 200 mg (0.59 mmol) of aminimide **4**, 10 mL of methanol, and 400 mg of acidic Dowex-50WX8-100 was stirred at 70 °C (oil bath temperature) for 24 h. The mixture was filtered and the filtrate was concentrated in vacuo and the residue was purified by chromatography over 15 g of silica gel (eluted with 7:3 hexane–ethyl acetate) to afford 120 mg (70%) of methyl oleate (**15**).

7.1.14. Attempted methanolysis of amide 13. A mixture of 200 mg (0.66 mmol) of amide **14**,[21] 10 mL of methanol, and 400 mg of acidic Dowex-50WX8-100 was stirred at 70 °C (oil bath temperature) for 24 h. The mixture was filtered and the filtrate was concentrated in vacuo to afford 190 mg (95%) of unchanged amide **13**.

7.1.15. Methanolysis of ethyl oleate (14). A mixture of 200 mg (0.65 mmol) of ethyl oleate (**14**), 10 mL of methanol, and 400 mg of acidic Dowex-50WX8-100 was stirred at 70 °C (oil bath temperature) for 12 h. The mixture was filtered and the filtrate was concentrated in vacuo to afford 200 mg of a 62:38 mixture of methyl oleate and ethyl oleate, respectively. When the reaction was analyzed after 5.5 h and four days, the ratios of methyl:ethyl esters were 11:89 and 96:4, respectively.

7.1.16. 2-Bromoethyl oleate (18). To a solution of 2.0 g (6.6 mmol) of oleoyl chloride in 50 mL of benzene were added sequentially 0.87 g (0.49 mL, 6.93 mmol) of 2-bromoethanol and 1.33 g (1.8 mL, 13.2 mmol) of triethylamine via syringe. The mixture was stirred at room temperature for 15 h, filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography over 60 g of silica (eluted with hexanes–ethyl acetate, 95:5) to give 2.42 g (94%) of ester **18** as yellow oil: IR (neat) 1743 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.8 (t, J=7 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.5–1.7 (m, 2H, CH_2CH_2CO), 1.8–2.0 (m, 4H, CH_2C=), 2.3 (t, J=7.3 Hz, 2H, CH_2CO), 3.5 (t, J=7.3 Hz, 2H, CH_2Br), 4.4 (t, J=7.3 Hz, 2H, CH_2O), 5.2–5.3 (m, 2H, CH=); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.1, 22.6, 24.8, 27.1, 27.1, 28.7, 29.0, 29.1, 29.3, 29.5, 29.6, 29.7, 31.8, 34.0, 63.5, 129.6, 129.9, 173.2 (two carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{20}H_{37}O_2{}^{79}BrNa$: m/z 411.1875, found: m/z 411.1862.

7.1.17. Ester 17. To a solution of 0.3 g (0.77 mmol) of bromide **18** in 1.5 mL of tetrahydrofuran was added 0.29 g (0.36 mL, 4.77 mmol) of 1,1-dimethylhydrazine in one portion. The mixture was stirred in a sealed tube with warming at 60 °C (oil bath temperature) for 5.5 h. The reaction was allowed to cool to room temperature and the solvent and excess 1,1-dimethylhydrazine were removed in vacuo to give

0.34 g (97%) of ester **17** as a yellow gel: IR (neat) 3214, 3111, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 0.8 (t, J=7 Hz, 3H, CH_3), 1.1–1.4 (m, 20H), 1.5–1.7 (m, 2H, CH_2CH_2CO), 1.8–2.0 (m, 4H, CH_2C=), 2.3 (t, J=7.3 Hz, 2H, CH_2CO), 3.6 (s, 6H, CH_3N), 4.0–4.1 (m, 2H, CH_2O or CH_2N), 4.5–4.6 (m, 2H, CH_2N or CH_2O), 5.2–5.3 (m, 2H, CH=); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.0, 22.5, 24.5, 27.0, 27.1, 28.96, 29.04, 29.13, 29.34, 29.54, 29.57, 31.7, 33.9, 56.9, 57.5, 67.5, 129.5, 129.8, 172.8 (two carbons were not observed due to suspected overlap of signals around δ 29); HRMS (ESI) calcd for $C_{22}H_{45}N_2O_2$: m/z 369.3481, found: m/z 369.3477. This material contained traces of contamination by both ^1H and ^{13}C NMR spectroscopies (see Supplementary data).

7.1.18. Methanolysis of aminimide 10. To a solution of 100 mg (0.22 mmol) of aminimide **10** in 5.0 mL of methanol was added 200 mg of Dowex-50X8-100 in one portion. The mixture was stirred at room temperature for 6.25 h, filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography over 20 g of silica gel (eluted with hexanes–ethyl acetate, 90:10) to give 42 mg (66%) of the methyl oleate (**15**) as a pale yellow liquid.

7.1.19. Methanolysis of ester 17. To a solution of 49 mg (0.11 mmol) of ester **17** in 2.5 mL of methanol was added 100 mg of Dowex-50X8-100 in one portion. The mixture was stirred at room temperature for 6.25 h, filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography over 15 g of silica gel (eluted with hexanes–ethyl acetate, 90:10) to give 25 mg (77%) of the methyl oleate (**15**) as a pale yellow liquid. ^1H NMR analysis prior to chromatography indicated a 95:5 mixture of **15** and **17**, respectively.

Acknowledgements

We thank the New Energy Development Organization (NEDO) of Japan for support of this research. One of us (B.E.C.) acknowledges support from the ACS Project SEED and NSF-REU programs.

Supplementary data

Selected experimental procedures, analytical data, and copies of ^1H and ^{13}C NMR spectra. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.08.023.

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14. Although the focus of this research is zwitterionic surfactants, we have also studied cationic surfactants as DR additives in 20% EG–80% water. For example, we have reported that a combination of EO12 (5 mM) and sodium salicylate (12.5 M) exhibits maximum % DRs of 60 and 58% at 20 and 0 °C, respectively.[12] To our knowledge there have been very few studies of drag-reducing agents in EG–water. These studies all employ zwitterionic or zwitterionic/anionic surfactant mixtures. For an amine oxide, $CH_3(CH_2)_7(CH{=}CH)$–$(CH_7)_8N(CH_2CH_2OH)_2O$, see: Haruki, N.; Inaba, H.; Horibe, A.; Tanaka, S. *Netsu Bussei* **2005**, *19*, 67 [CAN:143:250274]; For a patent that describes combinations of ammonium carboxylates [such as $CH_3(CH_2)_{17}N(CH_3)_2CH_2CO_2$] with dodecylbenzenesulfonates, monoalkyl sulfates, and related surfactants, see: Hellsten, M.; Oskarsson, H. World Intellectual Property Organization. WO 02/059228 A1 [CAN:137:142495].
15. This observation suggests that Dowex-50 might be used to sequester aminimides from DR solvent systems. Indeed, in a single experiment we have shown that 400 mg of Dowex-50 (H^+) will sequester at least 90% of **4** from 100 mL of a 6 mM solution of the aminimide in 20% EG–80% water. A pK_a of 5.3 has been reported for an aminimide derived from decanoic acid.[7]
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1979, *112*, 2145. It is notable that **10**, **14**, and **17** are stable to methanol (rt, 6.25 h) in the absence of Dowex-50. In addition, ethyl oleate (**14**) was recovered unchanged from treatment with Dowex-50 in methanol at rt for 4 h.

18. The procedures described herein were used to prepare over 1 kg of **4** for use in DR studies in a 1000-L flow system.[11]
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