Aziridines as Precursors for Chiral Amide-Containing Surfactants


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Optically active aziridines can be used as precursors in the synthesis of several enantiopure amide-containing surfactants. Acylation of the aziridines is a convenient method for both the activation of the aziridine ring and the introduction of the hydrocarbon chain. The regioselectivity of the ring-opening reactions using dibenzyl phosphate could be controlled by varying the reaction temperature. In this way both regiosomers of the phospholipid analogues could be obtained. In the course of these experiments, an unprecedented rearrangement of α-acylamino phosphotriesters was observed. A mechanism for this group exchange reaction was proposed based on the compared reactivities of related compounds and FT-IR spectroscopic data. Application of high pressures (12 kBar) for the ring opening of the activated aziridines with imidazole led to the efficient formation of the desired surfactant with complete regioselectivity.

Introduction

Following the discovery that phospholipid molecules can form tubular, rodlike, and even helical structures,1 it has been demonstrated that chiral synthetic surfactants can also be used to construct similar superstructures.2 The formation of these types of structures requires a high degree of organization within the aggregate in order to transfer the molecular chirality to the supramolecular level. Interconnecting the surfactant molecules by means of hydrogen bonding or π–π stacking was shown to be most useful in achieving and stabilizing these highly organized aggregates.2–4 In particular the formation of hydrocarbon-bonded chains of secondary amides, the so-called amide polymers, has been utilized successfully.4

A synthetic pathway for the preparation of amide-containing surfactants was developed in order to explore the use of amide functions in the construction of chiral aggregates. The synthesis of a series of new chiral surfactant molecules based on a C₃₅-skeleton having an amide-linked hydrocarbon chain on the C(2)-position was accomplished (Scheme 1). An ester or an ether group can be present on the primary position, and a variety of polar head groups can be introduced. A chiral precursor to which different hydrocarbon chains and polar head groups can be attached is required for the preparation of these lipids. In this respect the synthesis of phosphopeptides described by Okawa and co-workers is of interest.5,6 These authors used the chemistry of aziridines to introduce both the amide and phosphate moieties in successive steps. The acylation of an aziridine function served both as a peptide-coupling reaction and as an activation step for the introduction of the phosphate group by opening of the aziridine ring. This particular reaction offers prospects for the synthesis of amide-containing surfactants. Starting from a suitable aziridine, only two activation steps would suffice, in principle, for the introduction of both a hydrocarbon chain and a (protected) head group as depicted in Scheme 1 in a retrosynthetic manner.

Synthesis of N-Acylaziridines

An established procedure for the synthesis of chiral aziridines was employed,7–9 starting from the corresponding epoxides (Scheme 2). In this process the nucleophilic ring opening of the glycidyl derivatives 1 using sodium azide in 2-methoxylethanol/water10 gave a mixture of the two regioisomeric azido alcohols in 77–92% yield. The distilled mixture of azido alcohols was transformed into only one stereoisomer of the aziridine, however, by reaction with triphenylphosphine. In this so-called Staudinger reaction,11 both azido alcohols react

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with triphenylphosphine with concomitant extrusion of nitrogen to form a regiosomeric mixture of phosphazo compounds. Intramolecular addition of the hydroxyl group leads to the formation of oxazaphospholidines, which in related cases, have been isolated and characterized. The stereochemistry at either carbon atom in the aziridine ring is inverted compared with the stereochemistry at the respective products in good yields (64–92%).5

When dibenzyl phosphate was added to a solution of 5 in dichloromethane, a mixture of two products was obtained (Scheme 3). Both compounds were isolated using column chromatography and identified as the two regioisomers 6 and 7, which arise from nucleophilic attack on either (a) the primary C(1) or (b) the secondary C(2) carbon atom. The ratio of 6 and 7 amounted to 1:1.

Different reaction temperatures were used with the aim of improving the regioselectivity of the ring opening. It was found that the product ratio could be changed from 6:7 = 1:1 at room temperature to 6:7 = 6:1 at —15 °C. At temperatures lower than —30 °C, no reaction took place. After column chromatography the two regioisomers could always be isolated in pure form in a combined yield of 70–80%.

Surprisingly, it was found that butyrate derivatives 6b,c, after storage for several weeks, partially rearranged to give 7b,c (Scheme 3, path c), whereas pure 6a did not show any change during this period. Application of longer reaction times or temperatures higher than room temperature did not change the product ratio, indicating that under the conditions of phosphorylation no rearrangement takes place.

This rearrangement of 6b,c into 7b,c, after their isolation, can be avoided by immediate removal of the benzyl groups by catalytic hydrogenation and subsequent conversion into the respective disodium salts 8b,c (Scheme 4). Compound 8a and compounds 9 were obtained from 6a and 7, respectively, in an analogous manner.

Mechanistic Aspects of the Rearrangement of α-Acylamino Phosphate Triesters

The rearrangement in α-acylamino phosphate triesters 6b,c into 7b,c, described in the preceding section, has no precedent in the literature. It is important to note that no byproducts of any sort were observed during this rearrangement. That the phenoxy derivative 6a does not show this group exchange reaction is relevant for the mechanism. The findings suggest that a neighboring group participation of the butyrate ester group may be involved in the rearrangement. However, a nucleophilic displacement of the amido group by intramolecular attack of the ester carbonyl group either in an SN1 or SN2 fashion should lead to the formation of a dioxolenium ion, and as a consequence a product resulting from a shift of the butyrate to the C(2) carbon atom may be expected. No such product was observed, which makes the above

crystallization from ethyl acetate, the acylated aziridines 5 were isolated as white solids in almost quantitative yields.

Ring Opening of N-Acylaziridines with Dibenzyl Phosphate

The synthesis of phosphopeptides by ring opening of acylated aziridines using either dibenzyl phosphate or phosphoric acid as the reagent has been reported to lead to the respective products in good yields (64–92%).5

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The FT-IR spectra of a chloroform solution of this three-membered ring by the dibenzyl phosphate and accordingly the rearrangement. If the phosphorylation of 5 is carried out under acidic conditions since a 2-fold excess of dibenzyl phosphate is used. This is in agreement with the proposed mechanism, because intermolecular protonation of the ester carbonyl will prevent the formation of hydrogen bonds and accordingly the rearrangement.

In order to substantiate the role of hydrogen bonding, FT-IR spectra of a chloroform solution of 6b were recorded. This revealed the presence of two ester carbonyl vibrations at 1744 and 1729 cm⁻¹; the former is typical for a free ester function, and the latter is indicative of a hydrogen-bonded ester carbonyl.

Furthermore, the appearance of the amide I vibration at relatively high wavenumbers (1681 cm⁻¹) indicates the presence of an electron-rich amide group, supporting the increased nucleophilic character of the nitrogen atom. The FT-IR spectra of 6a showed the amide I vibration at high wavenumbers (1681 cm⁻¹); however, in addition a broadening of the P=O vibration was also observed, suggesting a hydrogen bond between the N—H of the amide and the P=O of the phosphate group. The formation of such a hydrogen bond would again enhance the nucleophilic character of the amide nitrogen atom. Attack on the primary carbon atom bearing the phosphate group is not possible due to the induced syn orientation of the phosphate with respect to the amide, and no rearrangement takes place (Scheme 4).

Ring Opening of N-Acylaziridines with Imidazole

The nucleophilic ring opening of acylated aziridines 5a and 5b by imidazole was first carried out by using sodium imidazolate in DMF at 80 °C. After 2 days, TLC analysis of the mixture showed the formation of several products. In both cases 11 could be obtained in only 12–15% yield, after column chromatography.

In spite of the poor nucleophilicity of imidazole,¹⁵ the use of this agent without the addition of a base was considered. A ring-opening reaction should proceed via the dipolar transition state 10 (Scheme 5). The formation of such a transition state will cause the solvent molecules to align their dipoles in a manner that electronically compensates the separation of charges. This will lead to a higher degree of organization and hence to a contraction of the volume of the reaction mixture. This negative volume of activation offers possibilities for the use of high pressure in accelerating product formation.¹⁶ A series of experiments was performed using equimolar amounts of 5c and imidazole in different solvents at 12 kBar.¹⁷ It was found that the reaction in chloroform showed the highest degree of conversion. However, even after 48 h, only 50% of the starting material had been consumed. The reaction was still incomplete after 4 days

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at 50 °C. The use of higher imidazole concentrations improved the rate of conversion, whereas the use of higher concentrations of 5c did not. These observations suggest that at higher pressures the temperature of aziridine 5c may limit the progress of the reaction. When the reaction was carried out with 2 equiv of imidazole in chloroform at 12 kBar and 55 °C for 2 days, the complete conversion of 5b,c into the desired imidazolyl surfactant 11 was accomplished, without the formation of any byproducts. Column chromatography of the depressurized reaction mixture resulted in the isolation of 11 in 30–50% yield.18

Concluding Remarks

The results described in this paper show that optically active aziridines can be used as precursors in the synthesis of several enantiopure amide-containing surfactants. Acylation of the aziridines is a convenient method for both the activation of the aziridine ring and the introduction of the hydrocarbon chain. The regioselectivity of the ring-opening reactions using dibenzyl phosphate was found to be satisfactory when low reaction temperatures were applied, and even complete when imidazole was used.

In the course of the synthesis of these phospholipids, an unprecedented rearrangement of α-acylamino phosphotriesters was observed. A mechanism for this group exchange reaction was proposed on the basis of the compared reactivities of related compounds and FT-IR spectroscopic data.

The fact that both regioisomers of the phospholipid analogues could be obtained expands the possibility to study the relation between molecular structure and the expression of chirality on the supramolecular level in two closely related substrates. A detailed study of the aggregation behavior of the chiral surfactants described above will be published elsewhere.

(18) A crude yield of ca. 90% was obtained. However, during the chromatographic procedure a considerable portion of the product was irreversibly bound to a silica.

Experimental Section

General. Most common procedures and instrumentation have been previously described. (2R)-(--)-Glycidyl butyrate was purchased from Aldrich Chemical Co.; (S)-Glycidyl-3-nitrobenzenesulfonate was a kind gift from Mr. Z. van Eupen (LGSS, Nijmegen). Solvents were dried and distilled prior to use according to standard procedures.20

(2R)-1-Azido-3-phenoxyprop-2-ol (2a) and (2S)-2-Azido-3-phenoxyprop-1-ol (3a). To a solution of (R)-phenoxymethylloxirane (1a)13 (10.0 g, 66.7 mmol) in 130 mL of methoxylethanol/water (10/3, v/v) were added sodium azide (8.67 g, 133 mmol) and ammonium sulfate (10.7 g, 80 mmol). After the mixture was stirred for 16 h, water (50 mL) and diethyl ether (90 mL) were added. The layers were separated, and the water layer was extracted with diethyl ether (2 × 50 mL). The combined organic layers were washed with brine and dried over Na2SO4. After evaporation of the solvent and distillation under reduced pressure, a colorless oil was obtained in 92% yield (bp 107 °C, 0.04 mmHg). From GLC the ratio of 2a and 3a was determined to be 7.7:1:1H NMR (CDCl3) 2a δ 1.98 (s, 1H), 3.46 (d, 2H, J = 5.1 Hz), 4.03 (m, 2H), 4.13 (m, 1H), 6.76–7.37 (m, 5H); 3a δ 1.98 (s, 1H), 2.77 (d, 2H, J = 5.2 Hz), 4.03 (m, 2H), 4.57 (m, 1H), 6.76–7.37 (m, 5H); IR (CCl4) 3440, 3020, 2860, 2100, 1580 cm–1.

(2R)-3-Azido-2-hydroxyprop-1-yl Butanoate (2b) and (2S)-3-Azido-2-hydroxyprop-1-yl Butanoate (3b). A mixture of 2b and 3b was synthesized starting from (2R)-(+-)-glycidyl butyrate ([α]D00 = –28.3 (c 1.0, CHCl3)) using the same procedure as described for compounds 2a and 3a. After distillation a colorless oil was obtained in 77% yield: bp 82 °C (0.05 mmHg):1H NMR (CDCl3) 2b δ 0.97 (t, 3H, J = 7.4 Hz), 1.67 (m, 2H), 2.69 (s, 1H), 2.34 (t, 2H, J = 7.4 Hz), 3.38 (m, 2H), 4.07 (m, 1H), 4.17 (m, 2H); 3b δ 0.96 (t, 3H, J = 7.4 Hz), 1.67 (m, 2H), 1.80 (s, 1H), 2.34 (t, 2H, J = 7.4 Hz), 3.51 (d, 2H, J = 5.4 Hz), 3.77 (d, 2H, J = 4.9 Hz), 5.02 (m, 1H); IR (CCl4) 3440, 2920, 2110, 1725 cm–1; MS (Cl+) m/z 188 (M + 1), 170 (18), 145 (3).

(2S)-(+)-2-(Phenoxymethyl)aziridine (4a). A mixture of (R)-2a and (S)-3a (5.8 g, 30.5 mmol) was added to a solution of triphenylphosphine (8.4 g, 32.1 mmol) in acetonitrile (150 mL). The reaction mixture was stirred until nitrogen evolution had ceased and subsequently heated under reflux for 6 h. After removal of the solvent under reduced pressure, the mixture was dissolved in hexane/ethyle acetate (1/1, v/v) from which triphenylphosphine oxide crystallized. Column chromatography (silica, methanol/ethyl acetate = 5/95, v/v) yielded the pure compound as a white solid in 97% yield: mp 61 °C; [α]D 0 D = 40.1° (c 1.0, CHCl3); 1H NMR (CDCl3) 4a δ 0.9-1.0 (br s, 1H), 1.5–2.0 (m, 4H), 2.2–2.5 (m, 3H), 3.9 (AA'X, 1H), 4.2 (AA'X, 1H); IR (CCl4) 3285, 2920, 2860, 2100, 1580 cm–1.

(2S)-(-)-2-(Phenoxymethyl)aziridine (4b). A colorless oil was obtained in 64% yield: [α]D00 = +9.6 (c 1.0, CHCl3); 1H NMR (CDCl3) δ 0.8 (t, 3H, J = 3.4 Hz), 1.93 (d, 1H, J = 6.0 Hz), 2.46 (m, 1H), 3.80–4.27 (m, 2H), 6.84–7.38 (m, 5H); IR (CCl4) 3300, 3050, 2950, 1580 cm–1; MS (Cl+) m/z 299 (2M + 1), 150 (M + 1), 133 (26), 105 (11), 94 (13), 77 (5).

(2S)-(+)-Aziridin-2-ylmethyl Butanoate (4b). Compound 4b was synthesized starting from a mixture of 2b and 3b using the same procedure as described for compound 4a. A colorless oil was obtained in 64% yield: [α]D00 = +9.6 (c 1.0, CHCl3); 1H NMR (CDCl3) δ 1.0 (t, 3H, J = 7.4 Hz), 0.9–1.0 (br s, 1H), 1.5–2.0 (m, 4H), 2.2–2.5 (m, 3H), 3.9 (AA'X, 1H), 4.2 (AA'X, 1H); IR (CCl4) 3285, 1735 cm–1.

(2S)-(-)-1-Octadecanoyl-2-(phenoxymethyl)aziridine (5a). At −10 °C a solution of stearoyl chloride (3.25 g, 10.7 mmol) in dichloromethane (100 mL) was added to a solution of 4a (1.60 g, 10.7 mmol) and triethylamine (1.91 g, 18.8 mmol) in dichloromethane (100 mL). After 3 h the reaction mixture was washed with 10% (w/w) aqueous citric acid, and the organic layer was dried over MgSO4. Evaporation of the solvent under reduced pressure and crystallization from ethyl acetate gave 5a as a white solid in 97% yield: mp 61 °C; [α]D00 = −25.5 (c 1.0, CHCl3); 1H NMR (CDCl3) δ 0.88 (t, 3H, J = 6.8 Hz).


Synthons for Chiral Amide-Containing Surfactants

Dibenzyl (2R)-3-(Butyryloxy)-1-(octadecanoylamino)propan-1-yl Phosphate (6a) and Dibenzyl (2R)-3-(Butyryloxy)-1-(octadecanoylamino)propan-1-yl Phosphate (9a). Phosphate triester 6a (225 mg, 0.32 mmol) was dissolved in methanol (100 mL) and subjected to hydrogenation using palladium on carbon as a catalyst. After the uptake of hydrogen had ceased the catalyst was filtered off over a short RP-18 column. The solution was concentrated under reduced pressure to a volume of approx. 50 mL, and 20 mL of water was added. This mixture was passed through an ion-exchange column (Dowex 50W×2, sodium form) and the methanol evaporated under reduced pressure. The white solid was precipitated from acidified water and dried. The yield: mp 145–147 °C; [α]_20D +24.5 (c 1.0, CHCl_3); H NMR (CDCl_3) δ 0.88 (t, 3H, J = 7.0 Hz), 0.92 (t, 3H, J = 7.4 Hz), 1.25 (m, 28H), 1.63 (m, 4H), 2.07 (t, 2H, J = 7.6 Hz), 2.22 (t, 2H, J = 7.6 Hz), 3.31–3.38 (m, 1H), 3.56–3.62 (m, 1H), 4.08–4.20 (m, 2H), 4.53–4.59 (m, 1H), 5.03 (d, 4H, J = 8.7 Hz), 6.73 (t, 1H, J = 5.3 Hz), 7.35 (m, 10H); IR (CCl_4) 3300, 2950, 2850, 1740, 1680, 1600 cm^-1; MS (FAB^+^) m/z 580 (M^+^ + Na^+^), 558 (M + 1). Anal. Calcd for C_{27}H_{40}O_5NaPO_4: C, 54.47; H, 8.45; N, 2.40. Found: C, 54.57; H, 8.35; N, 2.24.

Dibenzyl (2R)-3-Phenoxo-1-(octadecanoylamino)propan-1-yl Phosphate (8a). Phosphate triester 8a (264 mg, 0.32 mmol) was dissolved in methanol (100 mL) and subjected to hydrogenation using palladium on carbon as a catalyst. After the uptake of hydrogen had ceased the catalyst was filtered off over a short RP-18 column. The solution was concentrated under reduced pressure to a volume of approx. 50 mL, and 20 mL of water was added. This mixture was passed through an ion-exchange column (Dowex 50W×2, sodium form) and the methanol evaporated under reduced pressure. The white solid was precipitated from acidified water and dried. The yield: mp 145–147 °C; [α]_20D -20.1 (c 1.0, CHCl_3); IR (AgCl) 3300, 3080, 2910, 2840, 1630, 1600, 1550 cm^-1; MS (FAB^+^) m/z 580 (M^+^ + Na^+^), 558 (M + 1). Anal. Calcd for C_{27}H_{36}O_5NaPO_4: C, 54.63; H, 8.49; N, 2.36. Found: C, 54.57; H, 8.35; N, 2.24.

Dibenzyl (2R)-3-Propanoyl-2-(octadecanoylamino)propan-1-yl Phosphate (8b). Phosphate triester 8b (256 mg, 0.32 mmol) was dissolved in methanol (100 mL) and subjected to hydrogenation using palladium on carbon as a catalyst. After the uptake of hydrogen had ceased the catalyst was filtered off over a short RP-18 column. The solution was concentrated under reduced pressure to a volume of approx. 50 mL, and 20 mL of water was added. This mixture was passed through an ion-exchange column (Dowex 50W×2, sodium form) and the methanol evaporated under reduced pressure. The white solid was precipitated from acidified water and dried. The yield: mp 175–177 °C; [α]_20D -20.1 (c 1.0, CHCl_3); IR (AgCl) 3500–3100, 3080, 2920, 2860, 1640, 1600, 1550 cm^-1; MS (FAB^+^) m/z 580 (M^+^ + Na^+^), 558 (M + 1). Anal. Calcd for C_{27}H_{40}O_5NaPO_4: C, 60.33; H, 9.29; N, 2.55.

Dibenzyl (2R)-3-Propanol-1-(octadecanoylamino)propan-1-yl Phosphate (9b). Phosphate triester 9b (264 mg, 0.32 mmol) was dissolved in methanol (100 mL) and subjected to hydrogenation using palladium on carbon as a catalyst. After the uptake of hydrogen had ceased the catalyst was filtered off over a short RP-18 column. The solution was concentrated under reduced pressure to a volume of approx. 50 mL, and 20 mL of water was added. This mixture was passed through an ion-exchange column (Dowex 50W×2, sodium form) and the methanol evaporated under reduced pressure. The white solid was precipitated from acidified water and dried. The yield: mp 145–147 °C; [α]_20D +24.5 (c 1.0, CHCl_3); H NMR (CDCl_3) δ 0.88 (t, 3H, J = 7.0 Hz), 0.92 (t, 3H, J = 7.4 Hz), 1.25 (m, 28H), 1.63 (m, 4H), 2.07 (t, 2H, J = 7.6 Hz), 2.22 (t, 2H, J = 7.6 Hz), 3.31–3.38 (m, 1H), 3.56–3.62 (m, 1H), 4.08–4.20 (m, 2H), 4.53–4.59 (m, 1H), 5.03 (d, 4H, J = 8.7 Hz), 6.73 (t, 1H, J = 5.3 Hz), 7.35 (m, 10H); IR (CCl_4) 3300, 2950, 2850, 1740, 1680, 1600 cm^-1; MS (FAB^+^) m/z 580 (M^+^ + Na^+^), 558 (M + 1). Anal. Calcd for C_{27}H_{36}O_5NaPO_4: C, 54.63; H, 8.49; N, 2.36. Found: C, 54.57; H, 8.35; N, 2.24.
0.18 (silica, CH₃OH/H₂O/CHCl₃ = 39/10/67, v/v/v); [α]D° +1.0 (c 1.0, CHCl₃); IR (CHCl₃) 3400~3300, 2922, 2840, 1733, 1663, 1520 cm⁻¹; MS (FAB⁺) m/z 469 (M + 2), 326 (M − OPO₃Na₂).

Anal. Calcd for C₁₀H₁₆N₂O₇PNa₂·½H₂O: C, 47.89; H, 7.62; N, 4.60; (c 2.94). Found: C, 47.73; H, 7.96; N, 2.37.

**Disodium (2R)-3-Propanoyl-2-(octadecanoylamino)-propan-1-yl Phosphate 8c.** Compound 8c was synthesized starting from 6c using the same procedure as described for compound 8a. A white solid was obtained in 86% yield: Rf = 0.35 (silica, CH₂OH/H₂O/CHCl₃ = 39/10/67, v/v/v); [α]D° +5.2 (c 1.0, CHCl₃); IR (CHCl₃) 3292, 2933, 2845, 1727, 1637, 1551 cm⁻¹; MS (FAB⁺) m/z 552 (M + Na⁺), 574 (M + 1). Anal. Calcd for C₂₅H₄₈N₇O₇PNa₂·3H₂O: C, 49.58; H, 7.99; N, 2.31. Found: C, 49.31; H, 8.08; N, 2.29.

**Disodium (2R)-3-Propanoyl-1-(octadecanoylamino)-propan-1-yl Phosphate (9c).** Compound 9c was synthesized starting from 7c using the same procedure as described for compound 8a. A white solid was obtained in 84% yield: Rf = 0.20 (silica, CH₂OH/H₂O/CHCl₃ = 39/10/67, v/v/v); [α]D° +1.0 (c 1.0, CHCl₃); IR (CHCl₃) 3400~3300, 2922, 2840, 1733, 1663, 1520 cm⁻¹; MS (FAB⁺) m/z 552 (M + Na⁺), 574 (M + 1). Anal. Calcd for C₂₅H₄₈N₇O₇PNa₂·3H₂O: C, 54.44; H, 8.77; N, 2.54. Found: C, 53.96; H, 9.22; N, 2.52.

**(R)**-(-)-Butyric Acid 2-(Dodecanoylamino)-3-imidazol-1-ylpropyl Ester (11b). A 10 mL ampoule was charged with a chloroform solution containing 5b (215 mg, 0.66 mmol) and imidazole (90 mg, 1.32 mmol) and kept at 12 kbar for 4 days at 55 °C. After release of pressure the solvent was removed in vacuo, and the reaction mixture was subjected to flash column chromatography (silica, dichloromethane/ethanol/triethylamine = 92:7:1 v/v/v). After purification 11a was isolated as a colorless oil in 30% yield: [α]D° +9.6 (c 1.0, CHCl₃); 'H NMR (CDCl₃) δ 0.88 (t, 3H, J = 6.8 Hz), 0.98 (t, 3H, J = 7.4 Hz), 1.25 (m, 16H), 1.61 (m, 2H, J = 7.2 Hz), 1.66 (m, 2H, J = 7.4 Hz), 2.18 (t, 2H, J = 7.6 Hz), 2.35 (t, 2H, J = 7.4 Hz), 4.04 (dd, 1H, J = 14.8 Hz, J = 5.9 Hz), 4.17 (d, 2H, J = 5.0 Hz), 4.19 (dd, 1H, J = 14.2 Hz, J = 5.0 Hz), 4.40 (m, 1H, J = 3.3 Hz), 5.82 (d, 1H, J = 7.5 Hz), 6.94 (s, 1H), 7.08 (s, 1H), 7.49 (s, 1H); IR (CCl₄) 3300, 2910, 2850, 1735, 1670 cm⁻¹; MS (CI⁺) m/z 394 (M + 1), 326 (21), 306 (21). Anal. Calcd for C₃₅H₅₇NO₁₇: C, 65.64; H, 10.01; N, 10.43. Found: C, 65.62; H, 10.08; N, 10.30.

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**Supporting Information Available:** 'H-NMR spectra of compounds 2-4 and 6 (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the ACS; see any current masthead page for ordering information.

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