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Enantioselective Synthesis of Homosphingosine Derivatives from L-Aspartic Acid

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Abstract: The sterically demanding 9-phenylfluorenyl N-protection of a number of amino acids allows the formation of amino acid derived β-ketophosphonate reagents and their Horner–Wadsworth–Emmons olefination. In an attempt to develop a synthesis of D-erythro-homosphingosine in enantiopure form, we have shown that the reactivity of the intermediates is influenced by the distinctive conformational requirements of this large protecting group.

Key words: diastereoselectivity, enantioselectivity, sphingosine, ceramide

Sphingolipids constitute a major membrane component of eukaryotic cells, and important roles in cell recognition, differentiation, cell–cell contact and cell growth have been recognized. The backbone of sphingolipids is D-erythro-sphingosine (1; Figure 1); ceramides (2) are formed by acylation of the nitrogen with a fatty acid (RCOOH). More complex sphingolipids are formed by further addition of a polar head-group to the primary hydroxy group of sphingosine or ceramide.

We have previously developed a general and efficient synthesis of sphingosine based on a serine derived β-ketophosphonate. However, although this chemistry is reliable and robust enough to be used for sphingolipid synthesis and for several other targets, it still suffers from the fact that the original α-center of the amino acid remains vulnerable to epimerization. Although this epimerization can, in most cases, be suppressed to levels where it is not observed, in some highly sensitive cases these problems can be insurmountable.

9-Phenyl-9-fluorenyl (Pf) protection of the amino group has been shown to efficiently protect the carbon atom next to the nitrogen from epimerization, even in difficult cases. We therefore became interested in investigating whether the β-ketophosphonate chemistry we have developed for the Boc-protected amino acid derivatives can be translated to the corresponding Pf-protected amino acid derivatives. Towards this end, we chose a homosphingosine derivative as a first target molecule for testing the methodology.

Homosphingosine derivatives and homoceramides (Figure 2) have been the targets of only a few synthetic studies. A general synthetic approach to homoceramides could lead to the development of a new class of anticancer drugs, thus the synthesis of D-erythro-homosphingosine (3) was investigated in this work, with the aim of subsequently preparing a range of homoceramides.

![Figure 1](Image)

![Figure 2](Image)

We envisioned that D-erythro-homosphingosine (3) could be conveniently constructed from L-aspartic acid by internal asymmetric induction, whereby the two carboxy functionalities of L-aspartic acid could be transformed into the 2-amino-1,4-diol structure present in 3.

Our general strategy (Scheme 1) was to convert a protected L-aspartic acid into homoserine 5, and protect it as the N,O-acetal 6. The C-5 carbon would then be added with the formation of a β-ketophosphonate 7, and the E double bond as well as the aliphatic chain would be introduced through a modified Horner–Wadsworth–Emmons reaction to give enone 8. Selective reduction of the carbonyl and removal of the protecting groups would lead to the desired compound homosphingosine (3). The diastereoselectivity of the reduction was expected to be enhanced by bulky protecting groups: tert-butyl and 9-phenyl-9-fluorenyl of the amino group.

Anticipating difficulties during the phosphonation/chain-elongation of 6b because of sterice hindrance from the α-tert-butyl and 9-phenyl-9-fluorenyl groups, we initially...
conducted a model study with the L-alanine derived compound **11** (Scheme 2).

Crude **N-Pf**-protected **9** was directly esterified to give compound **10** in 42% yield as yellow crystals. An analytical sample was recrystallized from hexanes, and the X-ray crystal structure was determined (Figure 3).

Phosphonation of the model compound **10**, avoiding excess *n*-butyllithium [dimethyl methylphosphonate (5.5 equiv), *n*-BuLi (5.27 equiv)], gave **11** as a yellow oil in an acceptable, although low, yield of 52%. Encouraged by this finding, we embarked on the actual route with homoserine. **N-Pf-homoserine tert-butyl ester** (**5b**) was fully protected as the cyclic hemiaminal **6b** utilizing the method developed by Rapoport (Scheme 3).

Encouraged by the successful phosphonation of model compound **10**, we submitted **6b** to the conditions developed by Lee [dimethyl methylphosphonate (6.5 equiv) and *n*-BuLi (9.0 equiv)]. However, **6b** failed to react under these conditions, and led to only extensive decomposition under more forcing reaction conditions. Apparently, the steric hindrance caused by the tert-butyl and 9-phenylfluorenyl groups is enhanced by the rigid acetal ring of **6b**.

Having failed to form the β-ketophosphonate from acetal **6b**, we decided to opt for the less hindered methyl ester (Scheme 4). Thus, **α-methyl aspartate** (**16**) was converted into the crystalline α-methyl **N-Pf-aspartate** (**12**) (Figure 4). Borane reduction of **12** to the **N-Pf-homoserine methyl ester** (**5a**) was performed using the Alberg protocol. The starting material **12** needed to be heated and stirred for 2–3 days to yield 52% of **5a**. **N-O-Acetal protection of 5a** proceeded smoothly, giving **6a** in 85% yield. Simple recrystallization from hexanes gave pure **6a**. The crystal structure of **6a** is shown in Figure 5. It is noteworthy that both the methyl ester group and the bulky nitrogen pro-

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**Scheme 1**

**Scheme 2**  *Reagents and conditions:* i) Cl$_3$C(NH)OEtBu, CH$_2$Cl$_2$, 35% from L-Ala; ii) LiCH$_2$P(=O)(OMe)$_2$, THF, −78 °C, 52%.

**Scheme 3**

**Scheme 4**  *Reagents and conditions:* i) TMSCl, Et$_3$N, Pb(NO$_3$)$_2$, PfBr, CH$_2$Cl$_2$, r.t., 89%; ii) BH$_3$·THF, THF, 40 °C, 52%; iii) CH$_2$O, p-TsOH, THF, r.t., 85%; iv) LiCH$_2$P(=O)(OMe)$_2$, THF, −78 °C, 64%; v) tetradecanal, K$_2$CO$_3$, MeCN, r.t., 67%; vi) DIBAL-H, toluene, −78 °C, 55%.
Phosphonation of 6a with 3.3 equivalents of dimethyl methylphosphonate and 3.0 equivalents of n-BuLi gave 7 in 64% yield. Horner–Wadsworth–Emmons olefination gave the Z-olefin 8 in 67% yield.

DIBAL-H reduction\(^9\) of 8 in toluene was expected to give the desired anti-alcohol. However, presumably due to the conformational features of the ring substituents, the oxazinane underwent reductive ring opening, leaving a methyl group attached to the nitrogen (determined by HMBC 2D-NMR). The yield was modest, reaching only 55%, but only the anti diastereomer could be detected by \(^{1}H\) NMR after HPLC.\(^{19}\)

In conclusion, we have shown that the \(\beta\)-ketophosphonate/Horner–Wadsworth–Emmons olefination chemistry developed previously for Boc-protected serine derivatives can be successfully transferred to 9-phenylfluorenyl-protected amino acid derivatives for the synthesis of homosphingosine derivatives. Olefination followed by highly diastereoselective reduction of the enone were accompanied by the unwanted reductive cleavage of the hemiaminal moiety. The development of milder methods for the reduction of the sensitive enone will be reported in due course.

CH\(_2\)Cl\(_2\) and MeCN were distilled over CaH\(_2\), THF was distilled over sodium/benzophenone. MeOH over Mg(OMe)\(_2\), toluene over sodium, EtOH over Mg(OEt)\(_2\), and Et\(_3\)N over NaOH pellets. Pyridine was simply distilled. All other reagents were used as obtained from the supplier without further purification. Reactions were performed under an inert argon atmosphere, and anhydrous conditions were applied if dried solvents were used. Flash chromatography silica and TLC plates (silica gel 60 F\(_{254}\)) were obtained from Merck. TLC plates were visualized under UV irradiation (254 nm). Melting points were measured with a Gallenkamp melting point apparatus MFB 595 and are uncorrected. NMR spectra were recorded with a Bruker Avance 400 (\(^{1}H\) 400 MHz, \(^{13}C\) 100 MHz) instrument, and chemical shifts (\(\delta\)) are reported in ppm relative to TMS (\(\beta\) = 0 ppm). \(^{13}C\) NMR spectra were calibrated with the solvent signal. Infrared (IR) spectra were measured with a Perkin–Elmer Spectrum One instrument. Optical rotations were measured with a Perkin–Elmer Polarimeter 343, and elemental analyses (CHN) were performed with a Perkin–Elmer Elemental Analyzer 2400 CHN. The high resolution mass spectra (HRMS) were measured at the University of Oulu with a Micromass LCT mass instrument. HPLC was performed with the following conditions: Shandon Hypersil (5 \(\mu\)m, 250 \(\times\) 4.6 mm), Shandon Hyperprep (12 \(\mu\)m, 250 \(\times\) 4.6 mm) and Shandon Hyperprep (12 \(\mu\)m, 250 \(\times\) 10 mm); EtOAc–hexanes, 17–20%; flow rates: 1–5 mL/min.

\((S)\)-tert-Butyl 3-(9-Phenyl-9\(H\)-fluoren-9-yl)-1,3-oxazinane-4-carboxylate (6b)

Alcohol 5b (0.102 g, 0.25 mmol, 1.0 equiv) was dissolved in distilled THF (2 mL) under argon. Formaldehyde (0.3 mL, ~4 mmol, 16.0 equiv, 35–40% in H\(_2\)O) was added, followed by a catalytic amount of p-TsOH·H\(_2\)O. The mixture was stirred for 1 d, and quenched with sat. aq NaHCO\(_3\) (2 mL). The mixture was extracted with EtOAc (3 \(\times\) 10 mL), and the combined organic layers were washed with brine (5 mL), dried over MgSO\(_4\) and evaporated. Purification by flash chromatography (EtOAc–hexanes, 5%) yielded 6b.

Yield: 0.106 g (99%); colorless oil; \(R_f\) = 0.56 (EtOAc–hexanes, 50%); \([\alpha]_D^{20} +151\) (c 0.43, CHCl\(_3\)).
IR (NaCl): 3060–2834, 1724 cm⁻¹.

1H NMR (CDCl₃, 400 MHz): δ = 7.82–7.80 (m, 1 H, ArH), 7.70–7.67 (m, 1 H, ArH), 7.61–7.59 (m, 1 H, ArH), 7.52–7.13 (m, 10 H, ArH), 4.96 (d, J = 11.7 Hz, 1 H, N-CH₂), 4.84 (d, J = 11.7 Hz, 1 H, N-CH₂), 3.77 (m, 1 H, C=CH-O), 3.63 (m, 1 H, C=CH-H), 3.29 (m, 1 H, ROOC-CH₂-N), 1.44–1.31 (m, 2 H, CH₂-CH₂-OH)

IR (NaCl): 3295, 2954, 1713, 1258 cm⁻¹.


(2S)-tert-Butyl 1-[(9-Phenyl-9-fluoren-9-yl)amino]alaninate (10)
Crude (S)-N-[9-(9-phenylfluorenyl)]alanine (9; 2.1 g, 6.6 mmol) was dissolved in anhydrous CH₂Cl₂ (15 mL) under argon and the solution was transferred to the reaction flask using a syringe. O-tert-Butyl trichloroacetimidate (2.2 mL, 12.3 mmol) was added, and the solution was stirred for 3 d. The mixture was filtered and evaporated. Purification by flash chromatography (EtOAc–hexanes, 5%) MPLC (EtOAc–hexanes, 5%) and MPLC (EtOAc–hexanes, 45%) yielded colorless crystals for analytical purposes. Partial recrystallisation from CH₂Cl₂–hexanes and again from EtOAc–hexanes yielded colorless crystals for analytical purposes.

Yield: 0.97 g (89%); yellow foam; mp 128–129 °C; [α]D²⁰ = 297 (c 1.0, CHCl₃).

IR (KBrs): 3059–2956, 2636, 1736 cm⁻¹.

1H NMR (CDCl₃, 400 MHz): δ = 7.77–7.71 (m, 2 H, ArH), 7.46–7.22 (11, 1 H, ArH), 3.42 (s, 3 H, CH₃-OCH₃), 3.05 (dd, J = 4.9, 7.9 Hz, 1 H, MeOCH₂CH₂), 2.51 (dd, J = 9.7, 16.2 Hz, 1 H, CH₂-CH₂OCH₂), 2.18 (dd, J = 4.9, 16.2 Hz, 1 H, CH₂-CH₂OCH₂), 2.18 (dd, J = 4.9, 16.2 Hz, 1 H, CH₂-CH₂OCH₂).


(5)-Methyl 4-Hydroxy-2-[(9-phenyl-9H-fluoren-9-yl)amino]butanoate (5a)
To a stirred solution of (S)-methyl aspartate (4.0 g, 27 mmol, 1.0 equiv) in anhydrous CH₂Cl₂ (50 mL) was added TMSCl (3.7 mL, 29 mmol, 1.07 equiv) under argon. After 2 h, Et₂N (8.0 mL, 58 mmol, 2.15 equiv) was added and, after another 15 min, Pb(NO₃)₂ (5.96 g, 18 mmol, 0.67 equiv) and a solution of 9-bromo-9-phenylfluorene (11.57 g, 36 mmol, 1.33 equiv) in anhydrous CH₂Cl₂ (50 mL) were added. After stirring for 3 d, MeOH (14 mL) was added and, after another 15 min, the mixture was filtered and evaporated.

The viscous residue was partitioned between aq. citric acid (5%, 150 mL) and Et₂O (150 mL). The layers were separated and the aqueous layer was extracted with Et₂O (2 × 100 mL). The combined organic layers were washed with brine (60 mL), dried over MgSO₄ and evaporated. The residue was dissolved in Et₂O (70 mL) and extracted with sat. aq NaHCO₃ (5 × 30 mL). The aqueous layers were acidified with concd H₃PO₄ to pH 5 and extracted with Et₂O (2 × 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO₄ and evaporated to give 12. An analytical sample was recrystallised from CH₂Cl₂–hexanes and again from EtOAc–hexanes.

Yield: 9.3 g (89%); yellow foam; mp 128–129 °C; [α]D²⁰ = 297 (c 1.0, CHCl₃).

IR (KBrs): 3059–2956, 2636, 1736 cm⁻¹.

1H NMR (CDCl₃, 400 MHz): δ = 7.77–7.71 (m, 2 H, ArH), 7.46–7.22 (11, 1 H, ArH), 3.42 (s, 3 H, CH₃-OCH₃), 3.05 (dd, J = 4.9, 7.9 Hz, 1 H, MeOCH₂CH₂), 2.51 (dd, J = 9.7, 16.2 Hz, 1 H, CH₂-CH₂OCH₂), 2.18 (dd, J = 4.9, 16.2 Hz, 1 H, CH₂-CH₂OCH₂), 2.18 (dd, J = 4.9, 16.2 Hz, 1 H, CH₂-CH₂OCH₂).


(5)-Methyl 4-Hydroxy-2-[(9-phenyl-9H-fluoren-9-yl)amino]butanoate (5a) To a stirred solution of 12 (2.0 g, 5 mmol, 1.0 equiv) in anhydrous THF (10 mL) at –5 °C under argon, borane–THF (1.5 M in THF–Et₂O; 6.7 mL, 10 mmol, 2.00 equiv) was added dropwise. After stirring for 4 h, further borane (3.3 mL, 5 mmol, 1.00 equiv) was added and the cooling bath was removed. After 22 h, the mixture was heated to 40 °C for 45 h and the reaction was quenched by adding aq citric acid (10%, 30 mL). Et₂O (50 mL) was added, the layers were separated, and the aqueous layer was extracted with Et₂O (3 × 25 mL). The combined organic layers were washed with brine (30 mL), dried over Na₂SO₄ and evaporated. Purification twice with flash chromatography (EtOAc–hexanes, 10:20:50–5:75:100) then EtOAc–hexanes, 40% gave 14. Partial recrystallisation from benzene–hexanes yielded colorless crystals for analytical purposes.

Yield: 0.97 g (52%); yellow oil; mp 96–97 °C (Lit.16 96–97 °C).
(S)-Methyl 3-(9-Phenyl-9H-fluoren-9-yl)-1,3-oxazinan-4-yl)methyloxide (6a)

To a stirred solution of 5a (3.55 g, 9.5 mmol, 1.00 equiv) in distilled THF (80 mL), formaldehyde (11.5 mL, 152 mmol, 16.00 equiv, 35–40 wt% in H2O) and p-TsOH·H2O (0.133 g, 0.95 mmol, 10 equiv) were added under argon. The solution was stirred for 2 d then sat. aq NaHCO3 (20 mL) was added, which formed a white solid, and the mixture was extracted with EtOAc (3 × 30 mL). A little water was added to the aqueous layer to dissolve the white solid. The aqueous layer was extracted with EtOAc (2 × 30 mL) and the combined organic layers were washed with brine (30 mL), dried over Na2SO4 and evaporated. Recrystallisation of the mother liquor three times with EtOAc-cyclohexane, cyclohexane, and hexanes yielded three crops of 6a.

Yield: 3.109 g (85%); colorless to pale-yellow crystalline solid; mp 141 °C; [a]20 +253 (c 0.74, CHCl3).

IR (KBr): 3437, 2961–2850, 1732 cm–1.

1H NMR (CDCl3, 400 MHz): δ = 7.80–7.77 (m, 1 H, ArH), 7.70–7.68 (m, 1 H, ArH), 7.62–7.60 (m, 1 H, ArH), 7.48–7.15 (m, 10 H, ArH), 4.97 (d, J = 11.5 Hz, 1 H, CNPfCH2OCH2C), 4.86 (d, J = 11.5 Hz, CNPfCH2OCH2C), 3.79–3.74 (m, 1 H, CNPfCH2OCH2C), 3.64 (s, 3 H, CH3OC(=O), 3.65–3.58 (m, 2 H, CNPfCH2OCH2C, overlapping with the 3.64 singlet), 3.41–3.40 (m, 1 H, ROOCNCPfCH2OCH2C), 1.50–1.42 (m, 2 H, CHNPfCH2C), CH3C(=O), 3.79–3.74 (m, 1 H, CHNPfCH2C).

13C NMR (CDCl3, 100 MHz): δ = 173.5 (CO), 148.7, 147.7, 143.5, 140.7, 139.3, 128.6, 128.5, 128.4, 128.3, 127.8, 127.6, 127.4, 127.1, 125.6, 119.8, 119.7 (Ar), 78.0 and 77.9 (quat. aliph. and NCH2O), 64.4 (CH2O), 54.0 (ROOCNCPf), 51.8 (CH3OC(=O)), 25.7 (CHNPfCH2O).


(5)-Dimethyl (2-Oxo-2-[3-(9-phenyl-9H-fluoren-9-yl)-1,3-oxazinan-4-yl]ethyl)phosphonate (7)

To a stirred solution of dimethyl methylphosphonate (2.65 mL, 24.75 mmol, 3.30 equiv) in anhydrous THF (50 mL) at ~78 °C, n-BuLi (2.5 M in hexanes, 9.0 mL, 22.5 mmol, 3.00 equiv) was added over 15 min under argon. The solution was stirred for 10 min then 6a (2.874 g, 7.55 mmol, 1.00 equiv) in anhydrous THF (20 mL) was added over 35 min at ~78 °C (the reaction mixture turned slowly orange). The mixture was allowed to warm slowly to 0 °C over 3.6 h. The reaction was quenched with sat. aq NH4Cl (30 mL) and a little H2O was added to dissolve the formed solid. The mixture was extracted with EtOAc (3 × 30 mL) and the combined organic layers were dried over Na2SO4 and evaporated. Purification by flash chromatography (EtOAc–hexanes, 0→1→2→5%) gave 7 as a pale-yellow oil, which solidified on standing. The solid was recrystallised from EtOAc–hexanes for analytical purposes

Yield: 2.29 g (64%); white needles; mp 127 °C; [a]20 +191 (c 0.43, CHCl3).

IR (KBr): 3409, 3051–2847, 1713, 1271 cm–1.

1H NMR (CDCl3, 400 MHz): δ = 7.89–7.87 (m, 1 H, ArH), 7.72–7.69 (m, 1 H, ArH), 7.64–7.61 (m, 1 H, ArH), 7.49–7.18 (m, 10 H, ArH), 5.09 (dd, J = 1.65, 12.1 Hz, 1 H, NCH2O), 4.54 (dd, J = 12.1 Hz, 1 H, NCH2O), 3.76 [dd, J = 11.2, 18.6 Hz, 6 H, (CH3O)2P(=O)C], 3.65–3.50 (m, 2 H, CHNPfCH2OCH2C), 3.54 [dd, J = 15.3, 21.0 Hz, 2 H, PCH2(O)C(=O), overlapping with 3.65–3.50 (multiplets)], 3.37 [dd, J = 15.3, 21.0 Hz, 1 H, PCH2(O)C(=O)], 3.16 [br d, J = 5.9 Hz, CC(=O)CHNPfC], 1.51–1.47 (m, 1 H, CHNPfCH2CH2O), 1.11–1.01 (m, 1 H, CHNPfCH2CH2O).

13C NMR (CDCl3, 100 MHz): δ = 203.5 and 203.4 (CO), 148.6, 147.2, 142.3, 140.9, 139.6, 130.1, 128.7, 128.7, 128.6, 128.0, 127.7, 127.5, 127.1, 125.5, 120.0, 119.6 (Ar), 78.4 and 78.3 (quat. aliph. and NCH2O), 64.1 (CHNPfCH2CH2O), 60.5 [two peaks, CC(=O)CHNPfC], 52.94, 52.88, 52.85 and 52.79 [(CH3O)2P(=O)C], 37.5 and 36.2 [PCH2(C=O)C], 22.2 (CHNPfCH2CH2O).

Anal. Calcld for C39H49NO2: C, 83.08; H, 8.76; N, 2.48. Found: C, 83.19; H, 8.84; N, 2.44.

(5S,4S,E)-3-[Methyl(9-phenyl-9H-fluoren-9-yl)amino]nonadec-5-ene-1,4-diol (13)

Compound 8 (0.04 g, 0.07 mmol, 1.00 equiv) was dissolved in anhydrous toluene (3 mL) and cooled to ~78 °C under argon. DIBAL-H (1.0 M in toluene) was added in three portions: First portion (0.21 mL, 0.21 mmol, 3.00 equiv), after 22 min second portion (0.1 mL, 0.1 mmol, 1.40 equiv) and, after another 15 min, third portion (0.04 mL, 0.04 mmol, 0.57 equiv). 14 min after the last addition the reaction was quenched with acetone (1 mL) and the mixture was allowed to warm to r.t. A little H2O was added, followed by sat aq Na2SO4 (1.5 mL). After 15 min stirring, the mixture was filtered through Celite, and the Celite was washed with toluene. The filtered solution was concentrated under reduced pressure. H2O (2 mL) was added and the layers separated. The aqueous layer was extracted with Et2O (3 × 5 mL) and the combined organic layers were dried over Na2SO4 and evaporated. Purification by flash chromatography (EtOAc–hexanes, 25→75%) gave 13.
Yield: 0.022 g (55%); colorless oil; \( R_f = 0.45 \) (EtOAc–hexanes, 50%); \([\alpha]_D^{20} +246 \) (c 0.95, CHCl_3).

IR (NaCl): 3369, 2924, 2853 cm\(^{-1}\).

\( ^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta = 7.80-7.78 \) (m, 1 H, ArH), 7.65–7.62 (m, 1 H, ArH), 7.56–7.19 (m, 11 H, ArH), 5.65 (td, \( J = 6.8, 15.2 \) Hz, 1 H, CCH=CHCOHOC), 4.99 (dd, \( J = 8.2, 15.2 \) Hz, 1 H, CCH=CHCOHOC), 3.73 (t, \( J = 8.2 \) Hz, 1 H, CH=CHCH(OH)NPfCH3), 2.98–2.91 (m, 1 H, CCH(OH)H), 2.70–2.63 (m, 1 H, CCH=HOH), 2.57 (s, 3 H, CHNPfCH3), 2.25 (ddd, \( J = 3.7, 5.7, 9.1 \) Hz, 1 H, CH=CHCHNPfCH3), 1.95–1.89 (m, 2 H, \( \text{C}_3\text{H}_8\text{CH}(\text{CH})\text{CH} = \text{CH} \)), 1.35–1.15 (m, 22 H, CH\(_2\)(CH\(_3\))\(_3\)), 1.12–1.05 (m, 2 H, CHNPfCH\(_2\)(CH\(_3\))OH), 0.90 (t, \( J = 6.9 \) Hz, 3 H, \( \text{CH}_3\)(CH\(_3\))\(_3\)).

\( ^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta = 148.0, 146.6, 142.7, 141.3, 139.1 \) (Ar), 135.7 (CCH=CHCOH), 129.8 (CCH=CHCOH), 128.9, 128.6, 128.5, 124.7, 124.7, 127.4, 127.3, 126.9, 126.6, 126.1, 120.4, 119.8 (Ar), 77.8 (quat. aliph.), 73.9 (CCH=CHCOHCHNPfCH3C), 61.5 (CCH\(_2\)OH), 58.2 (CCHOHCHNPfCH3C), 32.3 (CCH=CH=CHC), 31.9 (aliphatic chain), 31.4 (CHNPfCH\(_2\)(CH\(_3\))OH), 30.4 (NCH\(_3\)), 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 28.9, 22.7 (aliphatic chain), 14.1 (CH\(_3\)).

HRMS: m/z [M + H]+ calcld for C\(_{39}\)H\(_{54}\)NO\(_2\): 568.4155; found: 568.4159.

Acknowledgment

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References


(12) X-ray crystallography was performed at the University of Jyväskylä with a Nonius Kappa CCD diffractometer. Crystal data for 10: Orthorhombic; \( P2_12_12 \), (No. 19); \( a = 9.0028 (3) \) Å, \( b = 9.4284 (3) \) Å, \( c = 25.0491 (8) \) Å; \( R_I = 0.0453, wR^2 = 0.0847 (I > 2\sigma(I)) \). (b) Monoclinic; \( P2_1 \), (No. 4); \( a = 9.8177 (7) \) Å, \( b = 8.8352 (5) \) Å, \( c = 11.3458 (8) \) Å, \( \beta = 92.366 (3)^\circ \); \( R_I = 0.0490, wR^2 = 0.0955 (I > 2\sigma(I)) \). (c) Orthorhombic; \( P2_12_12_1 \), (No. 19); \( a = 14.9329 (6) \) Å, \( b = 15.1950 (5) \) Å, \( c = 17.2261 (5) \) Å; \( R_I = 0.0573, wR^2 = 0.0936 (I > 2\sigma(I)) \). CCDC 255363–255365 contain the supplementary crystallographic data (excluding structure factors) for this paper. These data can be obtained online free of charge or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ UK [fax: (+44)1223336033; or deposit@ccdc.cam.ac.uk].


(19) The stereochemistry was assigned based on analogy with previous reductions, as well as on the coupling constants for similar compounds; see, for example, ref. 8d.