A Novel Class of Platelet Activating Factor (PAF) Antagonists. II.[1] Modification of the 2-Position of the Glycerol Backbone of PAF-Sulfonamide Isosteres

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In a continuing effort to obtain more potent platelet activating factor (PAF) antagonists, we tried to synthesize a series of PAF-sulfonamide isosteres in which the substituent at the 2-position was modified to an acetoxy equivalent other than the methoxy group. These modifications produced highly active PAF antagonists. Compound 3-[2-(5-methyl-2*H*-tetrazol-2-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium iodide (52) showed the most potent activity in the *in vitro* inhibitory effect on PAF-induced platelet aggregation in rabbit platelet-rich plasma (IC_{50} = 125 nM) and also in the *in vivo* protective effect on PAF-induced lethality in mice, with prolonged duration of action. Optically active enantiomers of this compound were synthesized and the (*S*)-(−)-isomer (IC_{50} = 87 nM) was found to be three times more potent that the (*R*)-(+)-isomer (IC_{50} = 289 nM), clearly exemplifying the enantioselectivity in the PAF-antagonist action of this novel compound.

Keywords platelet activating factor; receptor antagonist; platelet activating factor-sulfonamide isostere; optically active enantiomer; enantioselectivity; platelet aggregation; platelet activating factor-induced lethality

In the preceding paper,[1] we reported on the synthesis and biological activities of a novel class of platelet activating factor (PAF) analogues in which the charged phosphate and trimethylammonium moieties were replaced with sulfonamide and heterocyclic quarternary ammonium functionalities, respectively. These new PAF-sulfonamide analogues specifically consisted of 2-methoxy-3-propanol derivatives, bearing appropriate substituents, such as octadecylcarbamoyloxy, octadecylcarbamoylthio, hexadecyloxy and hexadecylthio, at the 1-position.

As Darmstoff phosphatidic acid analogues of this class (Darmstoff-sulfonamide isosteres), compounds with the *cis*-2,5-bis (hydroxymethyl)tetrahydrofuran backbone were also prepared. These sulfonamide derivatives proved to be potentially active as specific PAF antagonists from their *in vitro* inhibitory effect on PAF-induced platelet aggregation, demonstrating that they could be classified as a new family of PAF antagonists. PAF activity was found to be strongly affected by the nature of the substituent and its conformation at the 2-position of the glycerol backbone.

In continuing our efforts to obtain more potent PAF antagonists in this class of compounds, we tried to establish PAF antagonist activity specifically of the substituent at the 2-position of compound **3**, including its enantiospecificity.

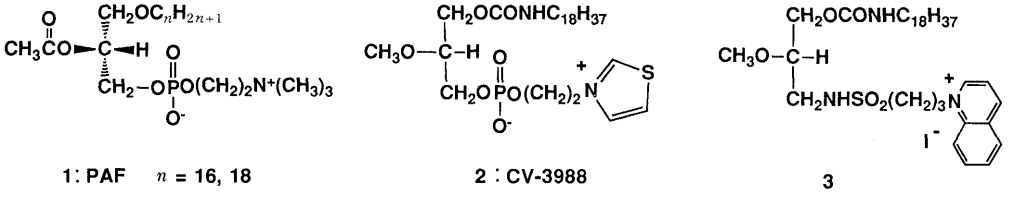


Fig. 1

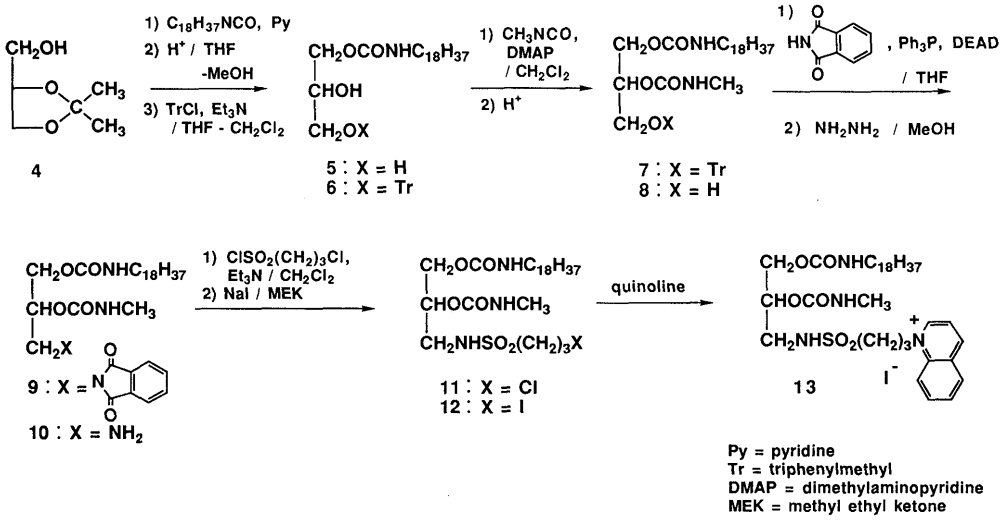


Chart 1

Among the compounds synthesized, compound **52**, which has a tetrazolyl group at the 2-position, was obviously superior to the hitherto described PAF-sulfonamide isosteres. Optically active enantiomers of **3** and **52** were also synthesized, and remarkable enantioselectivity was noted in the PAF antagonist action for compound **52**.

Chemistry As reported in the preceding paper, 3-[2-methoxy-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium iodide (**3**) showed strong PAF antagonist activity. In this paper, we explain how we tried to enhance this activity by replacing the methoxy group in this compound by other acetoxy equivalents such as methylcarbamoyloxy, methoxymethyl, 3-isoxazolyloxy, 2,2-spiro-tetrahydrofuranyl, methoxycarbonylamino, *tert*-butoxycarbonylamino, acetamide, methylureido, 3-methyl-1*H*-1,2,4-triazol-1-yl, 3-methyl-2*H*-1,2,4-triazol-2-yl, 5-methyl-1*H*-tetrazol-1-yl and 5-methyl-2*H*-tetrazol-2-yl groups.

2-Methylcarbamoyloxy derivative **13** was synthesized from solketal (**4**) as outlined in Chart 1.

Compound **4** was allowed to react with octadecyl isocyanate in pyridine, followed by deprotection of the acetonide group and tritylation of the primary hydroxy group of compound **5** to give **6**. Methylcarbamoylation of **6** with methyl isocyanate and 4-dimethylaminopyridine (DMAP),[2] followed by deprotection, gave **8**. The alcohol intermediate **8** was converted into primary amine **10** by the reaction of hydrazine (NH_2NH_2) with the phthalimide intermediate **9**, which was obtained by the Mitsunobu reaction of **8** with phthalimide, diethyl azodicarboxylate (DEAD) and triphenylphosphine (PPh_3) in tetrahydrofuran (THF). Coupling of the primary amine **10** with 3-chloropropanesulfonyl chloride in the presence of triethylamine (Et_3N) in dichloromethane (CH_2Cl_2), followed by iodination of the resulting product with sodium iodide (NaI) in methyl ethyl ketone (MEK), led to the corresponding iodoalkylsulfonamide derivative **12**. Compound **12** was finally allowed to react with quinoline to give **13**. As described in Chart 2, the alcohols, **14a**,[3] **14b**[4] and **14c**[5] were converted to the quinolinium derivatives **19**, **20** and **21**, respectively, according to the same procedure as described for the transformation of **8** to **13**.

The similar derivatives **30**, **31**, **32** and **33** were also synthesized from D,L-serine as outlined in Chart 3.

N-Tritylserine methyl ester (**22**)[6] was allowed to react

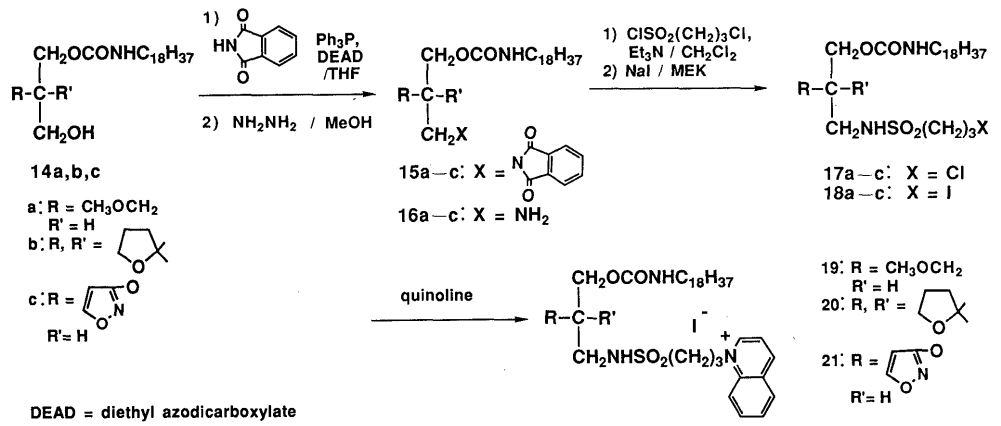


Chart 2

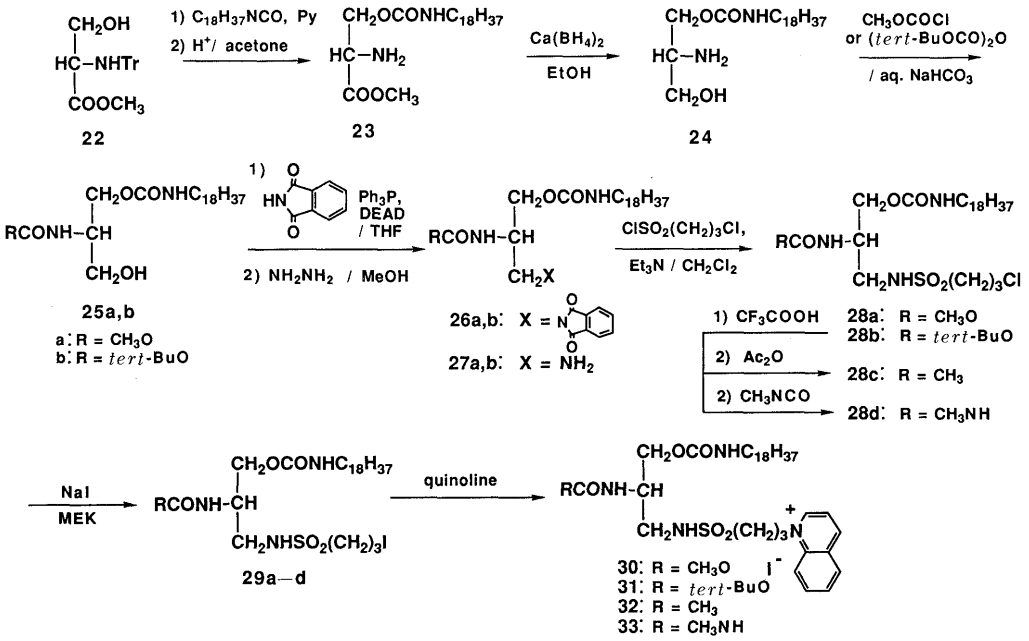


Chart 3

with octadecyl isocyanate in pyridine, followed by deprotection of the trityl group to give the amine **23**. Reduction of **23** to amino alcohol **24** was achieved by using calcium borohydride ($Ca(BH_4)_2$)[7] prepared from $NaBH_4$ and calcium chloride ($CaCl_2$) in EtOH. The 2-amino function of compound **24** was acylated with methyl chloroformate or di-*tert*-butyl dicarbonate to give **25a** or **25b** respectively, which were then converted into the 3-chloropropylsulfonyl derivatives **28a** and **28b** according to the procedure described previously for the preparation of **11** from **8**.

Deprotection of **28b** by the reaction with trifluoroacetic acid (CF_3COOH), followed by acylation of the 2-position with acetic anhydride (Ac_2O) or methyl isocyanate gave **28c** or **28d**, respectively. Compounds **28a—d** were converted into the final products **30—33** according to the procedure described for the conversion of **11** to **13**.

5-Methyltetrazole and 3-methyltriazole derivatives **44**, **45**, **52** and **53** were synthesized as outlined in Chart 4.

1-*tert*-Butyldimethylsilyloxy-3-trityloxypropan-2-ol (**35**), prepared from glycerol (**34**), was subjected to the Mitsunobu reaction with 5-methyltetrazole in THF to obtain a mixture of approximately 1:2 of the corresponding two regio-isomers of the 5-methyl-1*H*-tetrazol-1-yl derivative **36a** and the 5-methyl-2*H*-tetrazol-2-yl derivative **37a**. By the same Mitsunobu reaction with **35** and 3-methyltriazole in benzene,[8] followed by silica gel column chromatography, the corresponding two regio-isomers of 3-methyl-2*H*-1,2,4-triazol-2-yl derivatives **36b** and 3-methyl-1*H*-1,2,4-triazol-1-yl derivative **37b** were obtained in a 1:1 ratio. These compounds, **36a, b** and **37a, b**, whose structures were confirmed by nuclear Overhauser effect (NOE) experi-

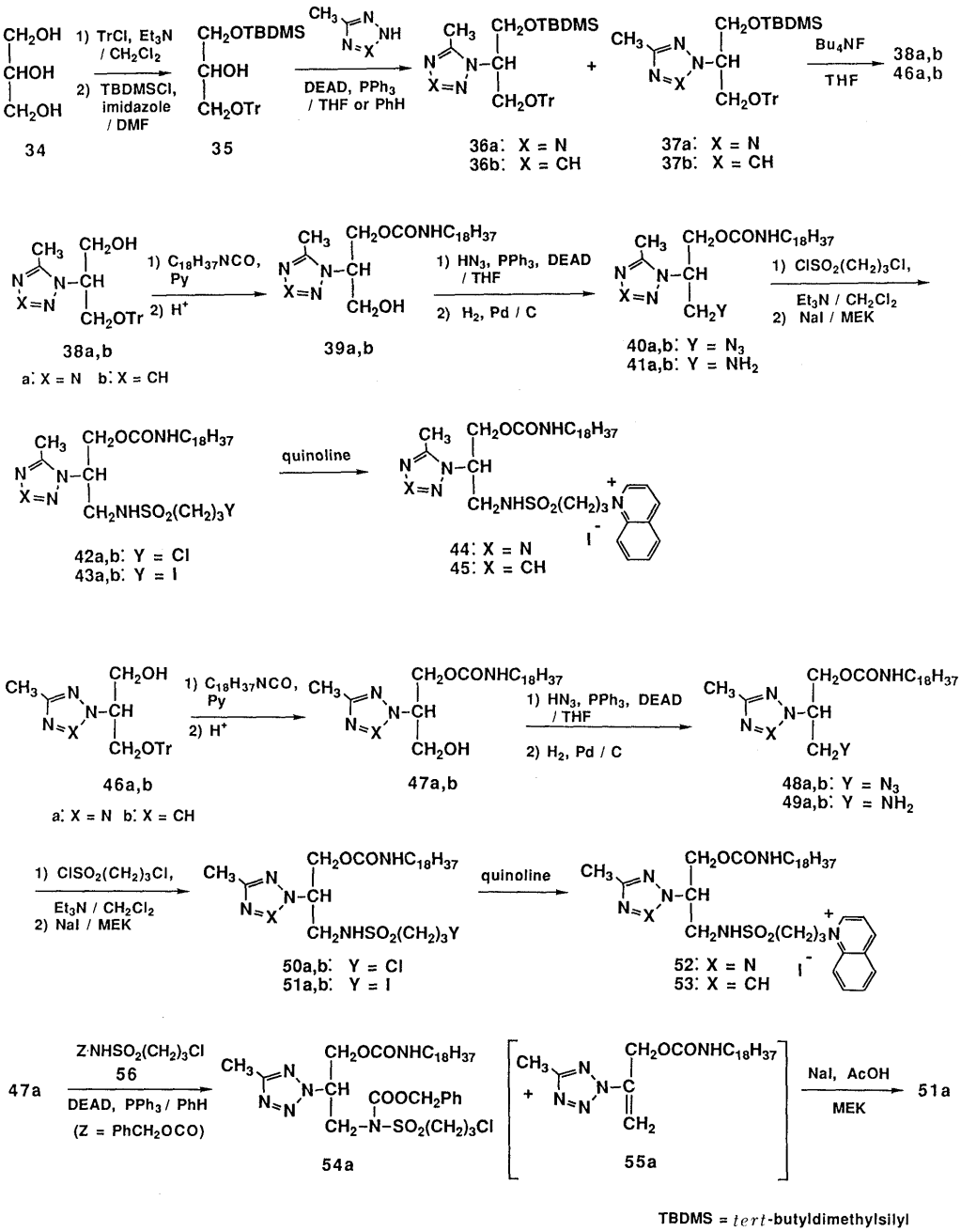


Chart 4

ments,[9] were selectively deprotected by treatment with tetrabutylammonium fluoride to obtain **38a, b** and **46a, b**, respectively. Compounds **38a, b** and **46a, b** were allowed to react with octadecyl isocyanate in pyridine and then deprotected by treatment with *p*-toluenesulfonic acid to afford **39a, b** and **47a, b**, respectively. Attempts to convert **39a, b** and **47a, b** into the corresponding primary amines under the Mitsunobu reaction condition using phthalimide as employed for the preparation of **10** were unsuccessful, giving only a dehydrated olefin similar to **55a**. This might be attributed to the increased acidity of the C-2 proton due to the presence of a more electronegative tetrazole and triazole ring compared to the methoxy group. This problem was solved by using HN_3 in the Mitsunobu reaction, followed by hydrogenation of the azido derivatives **40a, b** and **48a, b** to give corresponding primary amine derivatives **41a, b** and **49a, b**. These amine derivatives were converted into the final products **44**, **45**, **52** and **53** by the stepwise procedure described for the conversion of **10** to **13**. More conveniently, the glycerol derivative **47a** was converted to the sulfonamide intermediate **54a** by the Mitsunobu reaction with *N*-benzyloxycarbonyl-3-chloropropanesulfonamide (**56**), DEAD and PPh_3 in benzene in about an 80% yield, which is described in the preceding paper,[1] and formation of the elimination product **55a** was less than 20%. The sulfonamide intermediate **54a** was converted to **52** *via* the iodoalkylsulfonamide derivative **51a** which was obtained by a reaction with NaI in the presence of three molar equivalents of acetic acid (AcOH) in MEK.

These compounds were evaluated for their inhibitory activity of PAF-induced platelet aggregation of rabbit platelet-rich plasma, and we have found that substitution by a heterocyclic functional group at the 2-position resulted in a considerable increase in the antagonist activity in most cases. Among the substituent, the 5-methyl-2*H*-tetrazol-2-yl group was found to be especially effective (Table I).

In contrast to PAF and its unnatural enantiomer, each of which exhibit quite different biological activities, there have been several reports[10,11] in which some chiral-specific PAF antagonists with a PAF-like structure were reported to demonstrate almost equal antagonist activity in either enantiomeric form. But this is not always the case,[5] and the problem of the enantiospecificity of the substituent at the 2-position in PAF antagonist activity of PAF analogues remains to be clarified. For this purpose, we synthesized the optically active enantiomers of two representative PAF-sulfonamide isosteres, **3** and **52**, bearing the methoxy and 5-methyl-2*H*-tetrazol-2-yl function at the 2-position, respectively (Charts 5 and 6). Their racemates showed the most promising biological activities.

Commercially available, optically active glycerol acetonide (*S*)-(+)-**4** was directly converted into the corresponding *N*-protected sulfonamide intermediate (*S*)-**57** by the Mitsunobu reaction with **56**, PPh_3 and DEAD in THF. Stepwise deprotections of acetonide and the *N*-benzyloxycarbonyl groups of (*S*)-**57** by treatment with HCl, followed by catalytic hydrogenation over 5% Pd–C in THF–AcOH (1 : 1) led to (*S*)-(−)-**58**. The primary alcohol function of (*S*)-(−)-**58** was then selectively carbamoylated by treatment with octadecyl isocyanate in pyridine to give (*S*)-(−)-**59**. The secondary alcohol function of (*S*)-(−)-**59** was methylated with the Meerwein reagent, trimethyloxonium tetrafluoroborate [$(CH_3)_3O^+BF_4^-$], in CH_2Cl_2 to obtain optically active (*S*)-(−)-**60**. Similarly, the corresponding (*R*)-(+)-**60** was prepared starting from (*R*)-(−)-**4**. These optically active intermediates, (*S*)-(−)-**60** and (*R*)-(+)-**60**, were then transformed into the final products (*S*)-(−)-**3** and (*R*)-(+)-**3**, respectively, according to the procedures used for the conversion of **11** to **13**.

Preparation of optically active enantiomers bearing the 5-methyl-2*H*-tetrazol-2-yl function at the 2-position was achieved as illustrated in Chart 6. The optically active glycerol acetonide (*S*)-(+)-**4** was allowed to react with octadecyl isocyanate in pyridine followed by deprotection of its acetonide function by acid treatment to obtain (*R*)-(+)-**5**. After selective protection of the primary alcohol function by the trityl group, (*R*)-(+)-**5** was converted into the 2-(5-methyl-2*H*-tetrazol-2-yl) derivative (*S*)-**62** by the Mitsunobu reaction with 5-methyltetrazol, PPh_3 and DEAD in THF. This gave not only (*S*)-**62**, but also its 2-(5-methyl-1*H*-tetrazol-1-yl) isomer **63** (2 : 1 ratio), as well as considerable amounts of the corresponding rearranged

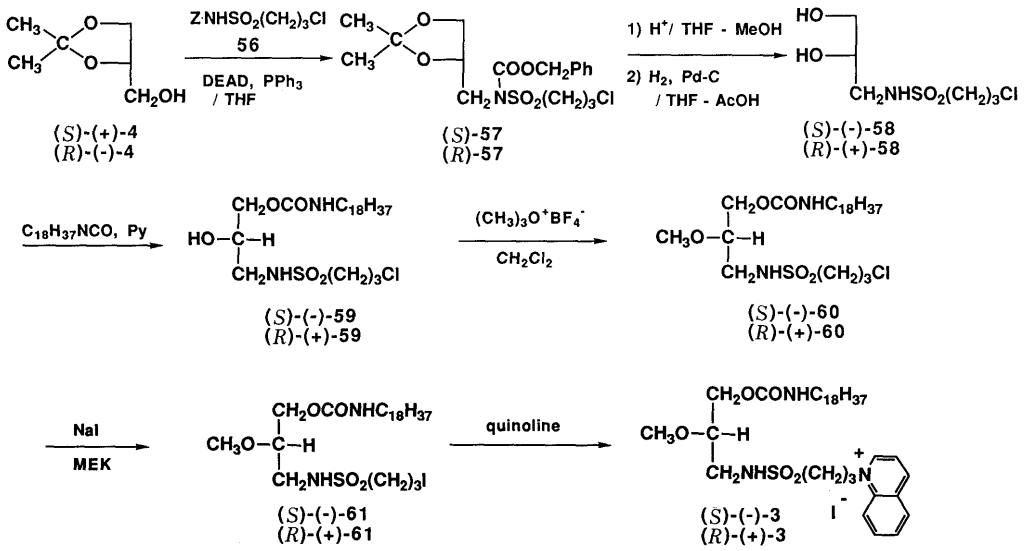


Chart 5

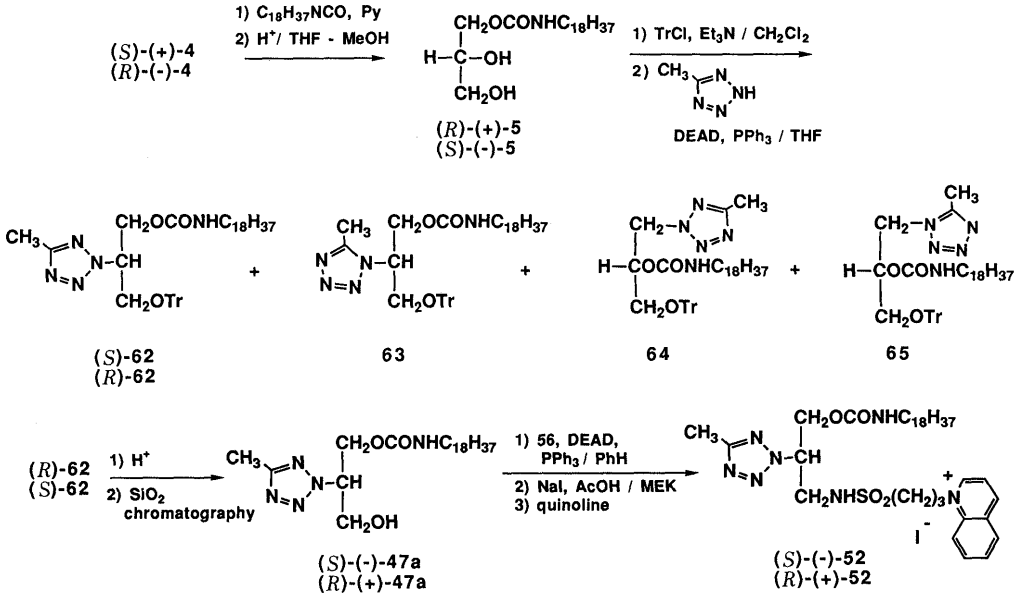


Chart 6

isomers **64** and **65**. After deprotection of the trityl group, the 5-methyl-2*H*-tetrazol-2-yl derivative (*S*)-(−)-**47a** was effectively separated by SiO_2 column chromatography from the mixture of these four isomeric pruducts. The optically active enantiomer (*S*)-(−)-**52** was obtained by the convenient transformation of (*S*)-(−)-**47a** as described in the preparation of the corresponding racemic **47a** into **52** *via* **54a**. By almost the same procedure, another enantiomer (*R*)-(+)-**52** could also be prepared from (*R*)-(−)-**4**.

Chiral purity was confirmed for the intermediates (*S*)-(−)-**59**, (*R*)-(+)-**59**, (*S*)-(−)-**47a**, and (*R*)-(+)-**47a** by the 200 MHz ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectra of their corresponding Mosher's ester[12] to be essentially pure within the limits of detection.

Results and Discussion

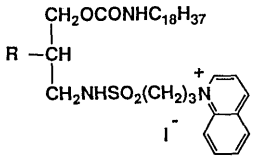
The *in vitro* PAF antagonist activity of the PAF-sulfonamide isosteres was evaluated as the inhibitory effect on PAF-induced platelet aggregation of rabbit platelet-rich plasma, which was examined using the method of Born.[13] The *in vivo* protective effect on PAF-induced lethality in mice was also evaluated. These results are summarized in Table I.

Among them, compound **52**, with the 5-methyl-2*H*-tetrazol-2-yl function at the 2-position, showed noticeably higher potencies than the other compounds, including CV-3988, in both *in vitro* and *in vivo* assays. Particularly interesting was the fact that its *in vivo* effect was found to still be prominent 60 min after i.v. administration. But it is regrettable that its oral absorption was fairly poor.

Enantioselectivity in the PAF-antagonist action was also evaluated for the sulfonamide derivatives **3** and **52** (Table II).

Although both of the optically active enantiomers of compound **3** exerted almost equal potency to that of the racemate, in the case of the compound **52**, the (*S*)-(−)-enantiomer with the same stereochemistry as the natural PAF was found to be three times more potent than the (*R*)-(+)-enantiomer. Our results suggest that the combination of a rather bulky substituent such as the 5-methyl-2*H*-tetrazol-2-yl group at the 2-position might fit better at the PAF-receptor site[14] to accommodate the acetoxy group as compared to a less bulky substituent such as the methoxy group. This resulted in the difference of activities between (*S*)-(−) and (*R*)-(+) isomers.

TABLE I. Inhibitory Activity on PAF-Induced Rabbit Platelet Aggregation and PAF-Induced Lethality in Mice



Compound	R	Platelet IC_{50}, μM[a]	Inhibition PAF-induced lethality[b] ED_{50} (mg/kg) 15 min	60 min
CV-3988 (**2**)		18.5	2.03	6.24
3	CH_3O–	0.65	6.15	>10
13	CH_3NHCOO–	0.33	0.296	3.71
19	CH_3OCH_2–	0.40	2.94	n.d.[c]
20	2,2-Spiro-tetrahydrofuranyl	0.385	0.61	4.91
21	3-Isoxazolyloxy	0.25	1.53	11.29
30	CH_3OCONH	0.533	1.73	>10
31	*tert*-BuOCONH	3.09	n.d.	
32	CH_3CONH–	1.83	n.d.	
33	$CH_3NHCONH$–	0.956	5.48	>10
44	5-Methyl-1*H*-tetrazol-1-yl	0.647	0.78	4.78
45	3-Methyl-1*H*-triazol-1-yl	0.535	n.d.	
52	5-Methyl-2*H*-tetrazol-2-yl	0.125	0.35	1.02
53	3-Methyl-2*H*-triazol-2-yl	0.387	0.61	2.47

a) Micromolar concentration of a test compound for 50% inhibition of rabbit platelet aggregation induced by C_{16}-PAF. *b*) Test compounds were given i.v. 15 and 60 min before a lethal dose of C_{16}-PAF (100 μg/kg). Survival of the mice was estimated 2 h after the PAF injection. *c*) Not done.

Conclusions

Among the PAF-sulfonamide analogues modified at the 2-position of compound **3**, 3-[2-(5-methyl-2*H*-tetrazol-2-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propyl-

Table II. Inhibitory Activity of Optically Active PAF Sulfonamide Isosteres on PAF-Induced Rabbit Platelet Aggregation

Compd.		IC_{50} (μM)[a]	Compd.		IC_{50} (μM)[a]
3	(*R*,*S*)-	0.655—0.676	**52**	(*R*,*S*)-	0.125—0.159
	(*S*)-(−)-	0.626		(*S*)-(−)-	0.087
	(*R*)-(+)-	0.772		(*R*)-(+)-	0.289

a) Micromolar concentration of a test compound for 50% inhibition of rabbit platelet aggregation induced by C_{16}-PAF.

quinolinium iodide (**52**) was found to have the most effective *in vitro* activity. This compound also showed high *in vivo* PAF-antagonist activity with prolonged duration as compared to CV-3988. Optically active enantiomers of this compound were also synthesized and remarkable enantioselectivity in the *in vitro* PAF antagonist action was observed, with the (*S*)-(−)-enantiomer being three times more effective than the (*R*)-(+)-enantiomer.

Experimental

Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere with dry solvents being used under anhydrous conditions and with anhydrous $MgSO_4$ being used as a drying agent for extracts. The organic solvents were removed by evaporation under reduced pressure with a rotary evaporator. Medium-pressure column chromatographies on Merck Lobar prepacked columns packed with LiChroprep Si 60 [size A (240—10 mm, 40—63 μm), size B (310—25 mm, 40—63 μm), and size C (440—37 mm, 40—63 μm)] were carried out for separation and purification of the products. Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Hitachi Model 260-10 spectrophotometer, and NMR spectra were determined on a Varian VXR-200 spectrometer.

1-Octadecylcarbamoyloxypropane-2,3-diol (5) To an ice-cooled and stirred solution of **4** (44 g, 0.33 mol) in pyridine (500 ml) were added octadecyl isocyanate (128 g, 0.43 mol) and DMAP (1.0 g) and the mixture was stirred at 50 °C overnight. After removal of the solvent, the residue was dissolved in ethyl acetate (AcOEt). The AcOEt layer was washed with saturated $KHSO_4$ and saturated NaCl, then concentrated *in vacuo*. The residue was dissolved in THF (600 ml)–methanol (MeOH) (100 ml). Conc. HCl (50 ml) was added to the mixture, and the mixture was allowed to stand at room temperature overnight. After passage through a pad of Celite to remove the insoluble material, the product was isolated by AcOEt extraction. The AcOEt layer was washed with H_2O, saturated $NaHCO_3$ and saturated NaCl. **5** (84.4 g, 88%) was obtained on reprecipitation from AcOEt as a colorless powder, mp 88—90 °C. *Anal.* Calcd for $C_{22}H_{45}NO_4$: C, 68.17; H, 11.70; N, 3.61. Found: C, 67.89; H, 11.44; N, 3.69.

1-Octadecylcarbamoyloxy-3-trityloxypropan-2-ol (6) To a stirred solution of **5** (80 g, 0.206 mol) in THF (800 ml) and CH_2Cl_2 (800 ml) were added trityl chloride (TrCl) (61.2 g, 0.22 mol) and Et_3N (40 ml, 0.29 mol), and the mixture was stirred at room temperature for 3 d. After removal of the solvent, the residue was dissolved in AcOEt. The AcOEt layer was washed with 1 N HCl, saturated $NaHCO_3$ and saturated NaCl. **6** (100 g, 77%) was obtained on reprecipitation from hexane as a colorless powder, mp 63—64 °C. *Anal.* Calcd for $C_{41}H_{59}NO_4$: C, 78.18; H, 9.44; N, 2.22. Found: C, 77.90; H, 9.40; N, 2.55.

2-Methylcarbamoyloxy-1-octadecylcarbamoyloxy-3-trityloxypropane (7) To an ice-cooled and stirred solution of **6** (1.26 g, 2.0 mmol) and DMAP (0.293 mg, 2.4 mmol) in CH_2Cl_2 (20 ml) was added methyl isocyanate (1.18 ml, 20 mmol), and the mixture was stirred at room temperature for 24 h. After removal of the solvent, the crude product was purified by silica gel column chromatography using an AcOEt–hexane (1 : 1) mixture as an eluent, and **7** (0.789 g, 59%) was obtained on reprecipitation from Et_2O–hexane as a colorless powder, mp 89—91 °C. NMR ($CDCl_3$) δ: 0.86 (3H, t, J=6.0 Hz), 1.28 (32H, br s), 2.74 (3H, d, J=6.0 Hz), 2.90—3.45 (4H, m), 4.24 (2H, d, J=6.0 Hz), 4.70 (2H, m), 5.10 (1H, m), 7.15—7.65 (15H, m). IR (Nujol): 3300, 1685, 1520, 1375, 1240, 1140 cm^{-1}.

2-Methylcarbamoyloxy-1-octadecylcarbamoyloxypropan-3-ol (8) To an ice-cooled solution of **7** (4.5 g, 6.68 mmol) in CH_2Cl_2 (45 ml) was added $BF_3 \cdot 2MeOH$ (1.08 ml, 9.96 mmol), and the mixture was stirred at room temperature for 4 h. The product was isolated by CH_2Cl_2 extraction. The CH_2Cl_2 layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl, and then dried and evaporated. The crude product was purified on reprecipitation from diethyl ether (Et_2O)–MeOH as a colorless powder, mp 92—93 °C. NMR ($CDCl_3$) δ: 0.86 (3H, t, J=6.0 Hz), 1.26 (32H, br s), 2.75 (3H, d, J=6.0 Hz), 2.80—3.45 (3H, m), 3.68 (2H, m), 4.25 (2H, d, J=6.0 Hz), 4.75—5.25 (3H, m). IR (Nujol): 3340, 1685, 1520, 1375, 1285, 1150, 1065 cm^{-1}. *Anal.* Calcd for $C_{24}H_{48}N_2O_5$: C, 64.83; H, 10.88; N, 6.30. Found: C, 64.50; H, 10.75; N, 6.35.

3-Amino-2-methylcarbamoyloxy-1-octadecylcarbamoyloxypropane (10) To an ice-cooled and stirred solution of **8** (2.0 g, 4.5 mmol), phthalimide (1.32 g, 9.0 mmol) and PPh_3 in THF (45 ml) was added DEAD (1.57 g, 9.0 mmol), and the mixture was stirred at room temperature overnight. After removal of the solvent, the residue was purified on reprecipitation from CH_2Cl_2–hexane to obtain crude phthaloyl derivative **9** (2.54 g). NMR ($CDCl_3$) δ: 0.86 (3H, t, J=6.0 Hz), 1.26 (32H, s), 2.68 (3H, d, J=6.0 Hz), 3.20 (2H, m), 3.80 (2H, m), 4.22 (2H, d, J=6.0 Hz), 4.80 (3H, m), 5.35 (1H, m), 7.65—7.85 (4H, m). IR (Nujol): 3340, 1705, 1685, 1520, 1365, 1300, 1255, 1180, 1135, 1105 cm^{-1}. To a solution of crude **9** (2.54 g, 4.42 mmol) in MeOH (25 ml) was added $NH_2NH_2 \cdot H_2O$ (0.336 g, 6.64 mmol), and the mixture was refluxed for 3 h. After removal of the insoluble material by passage through a pad of Celite, the filtrate was concentrated *in vacuo*. The crude residue was purified by silica gel column chromatography using a CH_2Cl_2–MeOH (9 : 1) mixture as an eluent, and **10** (1.21 g, 62%) was obtained on reprecipitation from CH_2Cl_2–hexane as a colorless powder, mp 91—92 °C. NMR ($CDCl_3$) δ: 0.86 (3H, t, J=6.0 Hz), 1.26 (32H, br s), 2.80 (3H, d, J=6.0 Hz), 2.92 (2H, m), 3.16 (2H, m), 4.22 (2H, d, J=6.0 Hz), 4.86 (3H, m). IR (Nujol): 3360, 1685, 1375, 1275 cm^{-1}. *Anal.* Calcd for $C_{24}H_{49}N_3O_4 \cdot 0.25H_2O$: C, 64.36; H, 11.07; N, 9.38. Found: C, 64.27; H, 10.89; N, 9.36.

3-(3-Chloropropylsulfonylamino)-2-methylcarbamoyloxy-1-octadecylcarbamoyloxypropane (11) To an ice-cooled and stirred solution of **10** (1.1 g, 2.48 mmol) and Et_3N (415 μl, 2.98 mmol) in CH_2Cl_2 (110 ml) was added 3-chloropropanesulfonyl chloride (362 μl, 2.98 mmol), and the mixture was stirred at room temperature for 4 h. The product was isolated by CH_2Cl_2 extraction. The CH_2Cl_2 layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using an AcOEt–hexane (1 : 1) mixture as an eluent, and **11** (1.23 g, 85%) was obtained on reprecipitation from CH_2Cl_2–hexane as a colorless powder, mp 102—103 °C. NMR ($CDCl_3$) δ: 0.84 (3H, t, J=6.0 Hz), 1.24 (32H, br s), 2.80 (3H, d, J=6.0 Hz), 2.24 (2H, m), 2.74 (3H, d, J=6.0 Hz), 2.95—3.50 (6H, m), 3.65 (2H, t, J=6.0 Hz), 4.20 (2H, d, J=6.0 Hz), 4.50 (1H, br s). IR (Nujol): 3320, 1685, 1530, 1275, 1155, 1115 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}ClN_3O_6S$: C, 55.50; H, 9.32; Cl, 6.07; N, 6.07; S, 5.49. Found: C, 55.42; H, 9.35; Cl, 6.13; N, 7.16; S, 5.34.

3-(3-Iodopropylsulfonylamino)-2-methylcarbamoyloxy-1-octadecylcarbamoyloxypropane (12) To a solution of **11** (1.22 g, 2.09 mmol) in MEK (60 ml) was added NaI (626 mg, 4.18 mmol), and the mixture was refluxed for 7 h, then cooled to room temperature and poured into 0.5 N $Na_2S_2O_3$. The product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using an AcOEt–hexane (1 : 1) mixture as an eluent, and **12** (1.15 g, 82%) was obtained on reprecipitation from CH_2Cl_2–hexane as a colorless powder, mp 97—99 °C. NMR ($CDCl_3$) δ: 0.90 (3H, t, J=6.0 Hz), 1.26 (32H, br s), 2.30 (2H, m), 2.80 (3H, d, J=6.0 Hz), 3.00—3.45 (8H, m), 4.22 (2H, d, J=6.0 Hz), 4.96 (3H, m), 5.52 (1H, m). IR (Nujol): 3320, 1685, 1530, 1375, 1320, 1260, 1140, 960 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}IN_3O_6S$: C, 47.99; H, 8.06; N, 6.22; S, 4.75. Found: C, 47.94; H, 8.04; I, 18.53; N, 6.25; S, 5.05.

3-[2-Methylcarbamoyloxy-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (13) Compound **12** (0.34 g, 0.5 mmol) was dissolved in quinoline (3 ml) and the mixture was allowed to stand at 50 °C for 8 h. After cooling to room temperature, Et_2O was added to the mixture and the precipitate was filtered. The precipitate was further purified by reprecipitation from Et_2O–MeOH to obtain **13** (255 mg, 63%) as a yellow powder, mp 137–139 °C. NMR ($CDCl_3$–CD_3OD) δ: 0.90 (3H, t, J=6.0 Hz), 1.30 (32H, br s), 2.76 (3H, s), 2.95—3.60 (11H, m), 4.20 (2H, m), 4.96 (1H, m), 5.48 (3H, m), 7.90—8.40 (4H, m), 8.65 (1H, d, J=9.0 Hz), 9.05 (1H, d, J=8.0 Hz), 10.02 (1H, d, J=5.0 Hz). IR (Nujol): 3360, 1690, 1390, 1260, 1160 cm^{-1}. *Anal.* Calcd for $C_{36}H_{61}IN_4O_6S$: C, 53.72; H, 7.64; I, 15.77; N, 6.96; S, 3.98. Found: C, 53.69; H, 7.51; I, 15.72; N, 6.96; S, 4.21.

2-Methoxymethyl-1-octadecylcarbamoyloxy-3-*N*-phthaloylaminopropane (15a) Yield 83%. Colorless powder. mp 84—85 °C (from MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.35—2.60 (1H, m), 3.12 (2H, q, J=7.0 Hz), 3.28 (3H, s), 3.41 (2H, d,

J=5.6 Hz), 3.79 (2H, d, J=7.0 Hz), 4.12 (2H, d, J=5.0 Hz), 4.67 (1H, br), 7.20—7.80 (2H, m), 7.80—7.95 (2H, m). IR ($CHCl_3$): 1773, 1712 cm^{-1}. *Anal.* Calcd for $C_{32}H_{52}N_2O_5$: C, 70.55; H, 9.62; N, 5.14. Found: C, 70.32; H, 9.57; N, 5.32.

3-Amino-2-methoxymethyl-1-octadecylcarbamoyloxypropane (16a) Yield 94%. Pale yellow wax. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 1.95—2.15 (1H, m), 2.18 (2H, s), 2.80 (2H, d, J=6.0 Hz), 3.16 (2H, q, J=6.0 Hz), 3.34 (3H, s), 3.35—3.55 (2H, m), 4.00—4.30 (2H, m), 4.89 (1H, br). IR ($CHCl_3$): 1716 cm^{-1}.

3-(3-Chloropropylsulfonylamino)-2-methoxymethyl-1-octadecylcarbamoyloxypropane (17a) Yield 94%. Colorless powder. mp 72—73 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.10—2.40 (3H, m), 3.00—3.30 (6H, m), 3.34 (3H, s), 3.35—3.55 (2H, m), 3.69 (2H, t, J=6.2 Hz), 4.06 (1H, ABX, J=14, 7.3 Hz), 4.18 (1H, ABX, J=14, 6.7 Hz), 4.81 (1H, t, J=6.0 Hz), 5.36 (1H, t, J=7.0 Hz). IR ($CHCl_3$): 1719, 1336 cm^{-1}. *Anal.* Calcd for $C_{24}H_{50}ClN_2O_6S$: C, 58.40; H, 9.98; Cl, 6.38; N, 5.05; S, 5.77. Found: C, 58.15; H, 9.89; Cl, 6.66; N, 5.17; S, 5.64.

3-(3-Iodopropylsulfonylamino)-2-methoxymethyl-1-octadecylcarbamoyloxypropane (18a) Yield 82%. Colorless wax. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.10—2.40 (3H, m), 3.05—3.30 (4H, m), 3.31 (2H, t, J=7.0 Hz), 3.35—3.55 (2H, m), 3.35 (3H, s), 4.06 (1H, ABX, J=12, 6.8 Hz), 4.18 (1H, ABX, J=12, 5.2 Hz), 4.86 (1H, t, J=6.0 Hz), 5.40 (1H, t, J=6.0 Hz). IR ($CHCl_3$): 1718, 1330 cm^{-1}.

3-[2-Methoxymethyl-3-(octadecylcarbamoyloxy)propylaminosulfonyl]-propylquinolinium Iodide (19) Yield 77%. Yellow powder. mp 55—60 °C (from Acetone–Et_2O). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.15—2.35 (1H, m), 2.60—2.85 (2H, m), 3.05—3.20 (2H, m), 3.15—3.35 (2H, m), 3.30 (3H, s), 3.44 (2H, d, J=6.0 Hz), 3.58 (2H, t, J=6.0 Hz), 3.95—4.25 (2H, m), 5.34 (1H, t, J=6.0 Hz), 5.61 (2H, t, J=8.0 Hz), 6.08 (1H, t, J=6.0 Hz), 7.98 (1H, t, J=8.0 Hz), 8.15—8.40 (3H, m), 8.71 (1H, d, J=9.4 Hz), 9.03 (1H, d, J=8.6 Hz), 10.31 (1H, d, J=5.8 Hz). IR ($CHCl_3$): 1710, 1332 cm^{-1}. *Anal.* Calcd for $C_{36}H_{62}IN_3O_5S \cdot 0.5H_2O$: C, 55.09; H, 8.09; I, 16.17; N, 5.35; S, 4.09. Found: C, 54.71; H, 8.07; I, 16.52; N, 5.42; S, 4.31.

2-Octadecyloxylcarbamoyloxymethyl-2-*N*-phthaloylaminomethyltetrahydrofuran (15b) Yield 94%. Coloroless powder. mp 91—92 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 1.75—2.10 (4H, m), 3.16 (2H, q, J=6.4 Hz), 3.84 (2H, s), 3.80—4.00 (2H, m), 4.03 (2H, s), 4.70—4.85 (1H, br s), 7.70—7.80 (2H, m), 7.80—7.90 (2H, m). IR ($CHCl_3$): 3440, 2920, 2845, 1710, 1510, 1465, 1420, 1390, 1205, 1060 cm^{-1}. *Anal.* Calcd for $C_{33}H_{52}N_2O_5$: C, 71.19; H, 9.41; N, 5.03. Found: C, 70.84; H, 9.28; N, 5.09.

2-Octadecyloxylcarbamoyloxymethyl-2-aminomethyltetrahydrofuran (16b) Yield 95%. Colorless wax. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.40—1.60 (2H, m), 1.72 (2H, s), 1.70—1.85 (2H, m), 1.85—2.05 (2H, m), 2.70 and 2.78 (2H, ABq, J=13.3 Hz), 3.16 (2H, q, J=6.6 Hz), 3.87 (2H, t, J=6.4 Hz), 4.04 (2H, s), 4.75—4.92 (1H, br s).

2-(3-Chloropropylsulfonylamino)methyl-2-octadecylcarbamoyloxymethyltetrahydrofuran (17b) Yield 84%. Colorless wax. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.40—1.60 (2H, m), 1.70—2.10 (4H, m), 2.20—2.38 (2H, m), 3.08—3.28 (6H, m), 3.68 (2H, t, J=6.2 Hz), 3.80—4.16 (4H, m), 4.78—4.90 (1H, br), 5.14 (1H, t, J=6.5 Hz). IR ($CHCl_3$): 3450, 2920, 2845, 1710, 1510, 1460, 1410, 1330, 1235, 1200, 1145, 1085, 1035, 710 cm^{-1}. MS *m/z*: 566 (M^+, Cl^{35}).

2-(3-Iodopropylsulfonylamino)methyl-2-octadecylcarbamoyloxymethyltetrahydrofuran (18b) Yield 76%. Colorless powder. mp 66.5—67.5 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.40—1.60 (2H, m), 1.70—2.10 (4H, m), 2.25—2.40 (2H, m), 3.10—3.24 (6H, m), 3.30 (2H, t, J=6.6 Hz), 3.84—4.14 (4H, m), 4.78—4.92 (1H, br), 5.14 (1H, t, J=6.4 Hz). IR ($CHCl_3$): 3450, 2925, 2850, 1710, 1510, 1460, 1405, 1330, 1215, 1145, 1100, 1035 cm^{-1}. MS *m/z*: 658 (M^+). *Anal.* Calcd for $C_{28}H_{55}IN_2O_5S$: C, 51.06; H, 8.42; I, 19.27; N, 4.25; S, 4.87. Found: C, 50.83; H, 8.34; I, 19.40; N, 4.50; S, 4.93.

3-[(Tetrahydro-(2-octadecylcarbamoyloxymethyl)furan-2-yl)methylaminosulfonyl]propylquinolinium Iodide (20) Yield 25%. Yellow powder. mp 57—62 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.6 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 1.68—2.00 (4H, m), 2.60—2.82 (2H, m), 3.11 (2H, q, J=6.6 Hz), 3.18—3.40 (2H, m), 3.50—3.70 (2H, m), 3.70—3.94 (2H, m), 3.99 (2H, s), 5.48 (1H, t, J=5.7 Hz), 5.54—5.72 (2H, m), 5.91 (1H, t, J=6.5 Hz), 7.98 (1H, t, J=7.5 Hz), 8.15—8.37 (3H, m), 8.70 (1H, d, J=9.2 Hz), 9.25 (1H, d, J=8.2 Hz), 10.34 (1H, d, J=5.0 Hz). IR ($CHCl_3$): 3400, 2930, 2850, 1710, 1460, 1430, 1325, 1230, 1140, 1040 cm^{-1}. *Anal.* Calcd for $C_{37}H_{62}IN_3O_5S \cdot 0.75H_2O$: C, 55.45; H, 7.99; I, 15.84; N, 5.24; S, 4.00. Found: C, 55.54; H, 8.01; I, not done; N, 5.53; S. 4.26.

3-(3-Chloropropylsulfonylamino)-2-(3-isoxazolyloxy)-1-octadecylcarbamoyloxypropane (17c) Yield 96%. Colorless powder. mp 63.5—65 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.20—2.35 (2H, m), 3.05—3.30 (2H, m), 3.40—3.60 (2H, m), 3.64 (2H, t, J=6.2 Hz), 4.40 (2H, d, J=4.4 Hz), 4.80—5.00 (2H, m), 5.36 (1H, t, J=7.0 Hz), 6.02 (1H, d, J=1.7 Hz), 8.18 (1H, d, J=1.7 Hz). IR ($CHCl_3$): 1727, 1338 cm^{-1}. *Anal.* Calcd for $C_{28}H_{52}ClN_3O_6S$: C, 56.59; H, 8.82; Cl, 5.97; N, 7.07; S, 5.40. Found: C, 56.06; H, 8.63; Cl, 6.03; N, 7.08; S, 5.70.

3-(3-Iodopropylsulfonylamino)-2-(3-isoxazolyloxy)-1-octadecylcarbamoyloxypropane (18c) Yield 85%. Colorless powder. mp 69—71.5 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.20—2.40 (2H, m), 3.05—3.30 (4H, m), 3.28 (2H, t, J=6.6 Hz), 3.40—3.60 (2H, m), 4.40 (2H, d, J=5.0 Hz), 4.85—5.00 (2H, m), 5.40 (1H, t, J=7.0 Hz), 6.06 (1H, d, J=1.8 Hz), 8.18 (1H, d, J=1.8 Hz). IR ($CHCl_3$): 1719 cm^{-1}. *Anal.* Calcd for $C_{28}H_{52}IN_3O_6S$: C, 49.05; H, 7.64; I, 18.51; N, 6.13; S, 4.68. Found: C, 48.71; H, 7.66; I, 18.75; N, 6.93; S, 4.94.

3-[2-(3-Isoxazolyloxy)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]-propylquinolinium Iodide (21) Yield 74%. Yellow amorphous powder. NMR ($CDCl_3$) δ: 0.90 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.35—1.55 (2H, m), 2.60—2.70 (2H, m), 3.10 (2H, q, J=6.0 Hz), 3.40—3.70 (4H, m), 4.28 (1H, ABX, J=12, 6.4 Hz), 4.38 (1H, ABX, J=12, 4.4 Hz), 4.85—5.00 (1H, m), 5.35 (1H, t, J=5.0 Hz), 5.54 (2H, t, J=7.0 Hz), 6.08 (1H, d, J=2.0 Hz), 6.45 (1H, t, J=6.0 Hz), 7.96 (1H, t, J=8.0 Hz), 8.10 (1H, d, J=2.0 Hz), 8.10—8.35 (3H, m), 8.70 (1H, d, J=10 Hz), 9.01 (1H, d, J=10 Hz), IR ($CHCl_3$): 1721, 1330 cm^{-1}.

***O*-Octadecylcarbamoylserine Methyl Ester (23)** To a stirred solution of *N*-tritylserine methyl ester (1.67 g) in DMF (10 ml) was added octadecyl isocyanate (2.0 g) and the mixture was allowed to stand at 85 °C for 16 h. The product was isolated by AcOEt extraction. The AcOEt layer was washed with H_2O then dried and evaporated. The product was purified by silica gel column chromatography using an AcOEt–hexane (2:3) mixture as an eluent, and *O*-octadecylcarbamoyl-*N*-tritylserine methyl ester (2.46 g, 83%) was obtained as an oil. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0 Hz), 1.25 (30H, s), 1.46 (2H, m), 2.78 (1H, d, J=10 Hz), 3.16 (2H, m), 3.19 (3H, s), 3.58 (1H, m), 4.21 (1H, dd, J=11.6 Hz), 4.37 (1H, dd, J=11.5 Hz), 4.69 (1H, t, J=11 Hz), 7.1—7.3 (9H, m), 7.45—7.6 (6H, m). IR (film): 3320, 1737 cm^{-1}.

To a stirred solution of the above compound (573 mg, 0.888 mmol) in acetone (15 ml) was added 10% HCl (5 ml), and the mixture was stirred at room temperature overnight. To the mixture was added saturated aqueous $NaHCO_3$, and the product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated NaCl, then dried and evaporated. The product was purified by silica gel column chromatography using an AcOEt–MeOH (9:1) mixture as an eluent, and **23** (276 mg, 75%) was obtained on reprecipitation from AcOEt–hexane as a colorless powder, mp 70—71 °C. NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.49 (2H, m), 1.78 (2H, s), 3.16 (2H, m), 3.73 (1H, m), 3.76 (3H, s), 4.31 (2H, d, J=5.0 Hz), 4.76 (1H, s). IR (Nujol): 3320, 1733, 1691 cm^{-1}.

2-Amino-1-octadecylcarbamoyloxypropan-3-ol (24) To a stirred solution of sodium borohydride ($NaBH_4$) (760 mg, 20.0 mmol) in EtOH (30 ml) at −40 °C was added $CaCl_2$ (1.11 g, 10.0 mmol), and the mixture was stirred at −20 °C for 1 h. To the mixture was added **23** (2.08 g, 5.02 mmol) in EtOH (50 ml) at −20 °C and the mixture was stirred at the same temperature for 3 h. The product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using a $CHCl_3$–MeOH (9:1) mixture as an eluent, and **24** (1.54 g, 81%) was obtained on reprecipitation from hexane as a colorless powder, mp 103—105 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.49 (2H, m), 1.73 (3H, s), 3.06 (1H, m), 3.17 (2H, m), 3.51 (2H, m), 4.08 (2H, d, J=5.0 Hz), 4.75 (1H, s). *Anal.* Calcd for $C_{22}H_{46}N_2O_3$: C, 68.35; H, 11.99; N, 7.25. Found: C, 67.93; H, 11.61; N, 6.81.

2-Methoxycarbonylamino-1-octadecylcarbamoyloxypropan-3-ol (25a) To a stirred solution of **24** (120 mg, 0.31 mmol) in 3 ml of 3.3% of aqueous Na_2CO_3, methyl chloroformate (117 mg, 1.24 mmol) was added and the mixture was stirred at room temperature for 6 h. The product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using AcOEt as an eluent, and **25a** (115 mg, 82%) was obtained on reprecipitation from hexane as a colorless powder, mp 84—85 °C. NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.50 (2H, m), 1.61 (1H, s), 3.07 (1H, br s), 3.18

(2H, m), 3.69 (3H, s), 3.86 (1H, br s), 4.20 (2H, d, J=5.0 Hz), 4.83 (1H, s), 5.23 (1H, d, J=7.0 Hz). IR (Nujol): 3450, 3320, 1687 cm^{-1}. *Anal.* Calcd for $C_{23}H_{48}N_2O_5$: C, 63.85; H, 11.18; N, 6.47. Found: C, 64.33; H, 10.86; N, 6.46.

2-*tert*-Butoxycarbonylamino-1-octadecylcarbamoyloxypropan-3-ol (25b) Instead of using methyl chloroformate, di-*tert*-butyl dicarbonate was used according to the procedure described above. Yield 93%. Colorless powder. mp 73—75 °C. NMR ($CDCl_3$) δ: 0.87 (3H, t, J=5.0 Hz), 1.26 (30H, s), 1.44 (9H, s), 1.56 (2H, m), 3.18 (2H, m), 3.63 (2H, m), 3.81 (1H, br s), 4.18 (2H, d, J=5.0 Hz), 4.78 (1H, br s), 5.20 (1H, br s). IR (Nujol): 3360, 1695 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}N_2O_5$: C, 66.63; H, 11.18; N, 5.76. Found: C, 66.35; H, 11.12; N, 5.87.

3-(3-Chloropropylsulfonylamino)-2-methoxycarbonylamino-1-octadecylcarbamoyloxypropane (28a) Yield 72%. Colorless powder. mp 99—101 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.0 Hz), 1.27 (30H, s), 1.50 (2H, m), 2.27 (2H, m), 3.1—3.4 (6H, m), 3.70 (3H, s), 3.6—3.8 (2H, m), 3.95 (1H, m), 4.19 (2H, d, J=5.0 Hz), 4.86 (1H, t, J=5.0 Hz), 5.45 (1H, t, J=5.0 Hz). IR (Nujol): 3350, 1696, 1048 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}ClN_3O_6S$: C, 55.51; H, 9.32; Cl, 6.07; N, 7.19; S, 5.49. Found: C, 55.07; H, 9.15; Cl, 6.24; N, 7.14.

2-*tert*-Butoxycarbonylamino-3-(3-chloropropylsulfonylamino)-1-octadecylcarbamoyloxypropane (28b) Yield 77%. Colorless powder. mp 112—115 °C. NMR ($CDCl_3$) δ: 0.89 (3H, t, J=5.0 Hz), 1.26 (30H, s), 1.45 (9H, s), 1.50 (2H, m), 2.29 (2H, m), 3.20 (6H, m), 3.69 (2H, t, J=6.0 Hz), 3.88 (1H, br s), 4.17 (2H, d, J=5.0 Hz), 4.80 (1H, t, J=4.0 Hz), 5.14 (1H, br s), 5.43 (1H, br s). IR (Nujol): 3340, 1699, 1689, 1309 cm^{-1}. *Anal.* Calcd for $C_{30}H_{60}ClN_3O_6S \cdot 0.7H_2O$: C, 56.71; H, 9.68; Cl, 5.58; N, 6.61; S, 5.05. Found: C, 56.66; H, 9.52; Cl, 5.27; N, 6.81; S, 5.27.

2-Acetamido-3-(3-chloropropylsulfonylamino)-1-octadecylcarbamoyloxypropane (28c) To a stirred solution of **28b** (252 mg, 0.402 mmol) in CH_2Cl_2 (5 ml) was added 0.5 ml of CF_3COOH in CH_2Cl_2 (2 ml) and the mixture was stirred at room temperature for 2 h. To the mixture was added saturated aqueous $NaHCO_3$, and the product was isolated by CH_2Cl_2 extraction. The CH_2Cl_2 layer was washed with saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using a $CHCl_3$–MeOH (9 : 1) mixture as an eluent, and 2-amino-3-(3-chloropropylsulfonylamino)-1-octadecylcarbamoyloxypropane (190 mg, 90%) was obtained on reprecipitation from AcOEt–hexane as a colorless powder, mp 86—88 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.0 Hz), 1.26 (30H, s), 1.50 (2H, m), 2.20 (2H, br s), 2.30 (2H, m), 3.16 (6H, m), 3.69 (2H, t, J=6.0 Hz), 4.09 (1H, br s), 4.88 (1H, br s). *Anal.* Calcd for $C_{25}H_{52}ClN_3O_4S$: C, 57.06; H, 9.96; Cl, 6.74; N, 7.99; S, 6.09. Found: C, 57.09; H, 9.81; Cl, 6.56; N, 8.10; S, 6.17. To a stirred solution of the above compound (501 mg, 0.952 mmol) and Ac_2O (194 mg, 1.90 mmol) in CH_2Cl_2 (15 ml) was added pyridine (0.77 ml, 9.52 mmol) in CH_2Cl_2 (2 ml), and the mixture was stirred at room temperature for 2 h. The product was isolated by AcOEt extraction. The AcOEt layer was washed with 1 N HCl, saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using a $CHCl_3$–MeOH (10 : 1) mixture as an eluent, and **28c** (459 mg, 85%) was obtained on reprecipitation from AcOEt as a colorless powder, mp 110—112 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.50 (2H, m), 2.02 (3H, s), 2.28 (2H, m), 3.1—3.3 (6H, m), 3.69 (2H, t, J=6.0 Hz), 4.1—4.3 (3H, m), 4.91 (1H, t, J=6.0 Hz), 5.72 (1H, br s), 6.48 (1H, d, J=6.0 Hz). IR (Nujol): 3340, 3295, 1690, 1650, 1310, 1144 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}ClN_3O_5S$: C, 57.07; H, 9.58; Cl, 6.24; N, 7.39; S, 5.64. Found: C, 56.80; H, 9.43; Cl, 6.33; N, 7.44; S, 5.70.

3-(3-Chloropropylsulfonylamino)-2-(3-methylureido)-1-octadecylcarbamoyloxypropane (28d) Instead of using Ac_2O, methylisocyanate was used according to the procedure described above. Yield 88%. Colorless powder. mp 87—90 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s). 1.50 (2H, m), 2.28 (2H, m), 2.77 (3H, s), 3.1—3.3 (6H, m), 3.68 (2H, t, J=7.0 Hz), 4.05 (1H, br s), 4.15 (2H, m), 5.04 (1H, br s), 5.51 (1H, br s), 6.11 (1H, br s). IR (Nujol): 3300, 1692, 1313, 1144 cm^{-1}. *Anal.* Calcd for $C_{27}H_{55}ClN_4O_5S$: C, 55.60; H, 9.50; Cl, 6.08; N, 9.61; S, 5.50. Found: C, 55.17; H, 9.42; Cl, 6.18; N, 9.57; S, 5.36.

3-(3-Iodopropylsulfonylamino)-2-methoxycarbonylamino-1-octadecylcarbamoyloxypropane (29a) Yield 95%. Colorless powder. mp 93 °C. NMR ($CDCl_3$) δ: 0.90 (3H, t, J=4.0 Hz), 1.28 (30H, s), 1.51 (2H, m), 2.34 (2H, m), 3.1—3.4 (8H, m), 3.71 (3H, s), 3.97 (1H, m), 4.19 (2H, s), 4.85 (1H, s), 5.43 (1H, s). IR (Nujol): 3340, 1697, 1144 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}IN_3O_6S$: C, 47.99; H, 8.06; I, 18.78; N, 6.22; S, 4.74. Found: C, 47.74; H, 7.91; I, 18.50; N, 6.22; S, 4.91.

3-[2-Methoxycarbonylamino-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (30) Yield 70%. Yellow powder. mp 70—74 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.0 Hz), 1.25 (30H, s), 1.50 (2H, m), 2.72 (2H, br s), 3.12 (2H, m), 3.35 (2H, br s), 3.59 (3H, s), 4.00 (1H, br s), 4.15 (2H, br s), 5.45 (1H, br s), 5.55 (2H, br s), 5.86 (1H, br s), 6.25 (1H, br s), 8.00 (1H, t, J=8.0 Hz), 8.20 (1H, m), 8.29 (2H, m), 8.69 (1H, d, J=8.0 Hz), 9.01 (1H, d, J=8.0 Hz), 10.19 (1H, s). IR (Nujol): 3320, 1702, 1143 cm^{-1}.

2-*tert*-Butoxycarbonylamino-3-(3-iodopropylsulfonylamino)-1-octadecylcarbamoyloxypropane (29b) Yield 89%. Colorless powder. mp 96—98 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.45 (11H, s), 2.32 (2H, m), 3.1—3.3 (6H, m), 3.31 (2H, t, J=7.0 Hz), 3.89 (1H, br s), 4.17 (2H, br s), 4.82 (1H, br s), 5.15 (1H, br s), 5.44 (1H, br s). IR (Nujol): 3370, 3270, 1692, 1143 cm^{-1}. *Anal.* Calcd for $C_{30}H_{60}IN_3O_6S$: C, 50.20; H, 8.43; N, 5.85; S, 4.47. Found: C, 50.40; H, 8.44; N, 5.91; S, 4.47.

3-[2-*tert*-Butoxycarbonylamino-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (31) Yield 69%. Yellow powder. mp 78—82 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.39 (9H, s), 1.50 (2H, m), 2.74 (2H, m), 3.13 (2H, m), 3.32 (2H, t, J=7.0 Hz), 3.58 (2H, t, J=7.0 Hz), 3.94 (1H, m), 4.15 (2H, s), 5.45 (1H, s), 5.59 (1H, t, J=8.0 Hz), 6.19 (1H, s), 7.99 (1H, t, J=9.0 Hz), 8.17 (1H, dd, J=5.0, 10.0 Hz), 8.23 (2H, d, J=8.0 Hz), 8.65 (1H, d, J=5.0 Hz), 8.97 (1H, d, J=5.0 Hz), 10.33 (1H, d, J=5.0 Hz). IR (Nujol): 3360, 1693, 1323, 1148 cm^{-1}. *Anal.* Calcd for $C_{39}H_{67}IN_4O_6S \cdot 0.7H_2O$: C, 54.50; H, 8.02; I, 14.76; N, 6.52; S, 3.73. Found: C, 54.87; H, 8.13; I, 14.12; N, 6.64; S, 3.94.

2-Acetamido-3-(3-iodopropylsulfonylamino)-1-octadecylcarbamoyloxypropane (29c) Yield 92%. Colorless powder. mp 101—102 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.50 (2H, m), 2.02 (3H, s), 2.31 (2H, m), 3.1—3.3 (4H, m), 3.15 (2H, t, J=7.0 Hz), 3.30 (2H, t, J=7.0 Hz), 4.17 (3H, m), 4.93 (1H, t, J=5.0 Hz), 5.74 (1H, t, J=5.0 Hz), 6.49 (1H, br s). IR (Nujol): 3320, 3280, 1690, 1657, 1320, 1268, 1140 cm^{-1}. *Anal.* Calcd for $C_{27}H_{54}IN_3O_5S$: C, 49.16; H, 8.25; N, 6.37; S, 4.86. Found: C, 49.13; H, 8.21; N, 6.27; S, 4.92.

3-[2-Acetamido-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (32) Yield 82%. Yellow powder. mp 77—82 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.48 (2H, m), 2.01 (3H, s), 2.68 (2H, m), 3.10 (2H, m), 3.33 (2H, m), 3.56 (2H, m), 4.12 (2H, m), 4.28 (1H, m), 5.54 (2H, m), 6.56 (1H, m), 7.19 (1H, d, J=7.0 Hz), 7.99 (1H, t, J=7.0 Hz), 8.17 (1H, dd, J=6.0, 7.0 Hz), 8.25—8.40 (2H), 8.70 (1H, d, J=9.0 Hz), 8.99 (1H, d, J=5.0 Hz), 10.13 (1H, d, J=6.0 Hz). IR (Nujol): 3335, 1692, 1600, 1310, 1272, 1142 cm^{-1}. *Anal.* Calcd for $C_{36}H_{61}IN_4O_5S \cdot 0.3H_2O$: C, 54.44; H, 7.82; N, 7.05; S, 4.04. Found: C, 54.65; H, 8.07; N, 7.14; S, 4.13.

3-(3-Iodopropylsulfonylamino)-2-(3-methylureido)-1-octadecylcarbamoyloxypropane (29d) Yield 96%. Colorless powder. mp 87—89 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.0 Hz), 1.26 (30H, s), 1.50 (2H, m), 1.69 (1H, br s), 2.31 (2H, m), 2.77 (3H, s), 3.1—3.3 (4H), 3.14 (2H, t, J=7.0 Hz), 3.30 (2H, t, J=7.0 Hz), 4.05 (1H, m), 4.14 (2H, d, J=4.0 Hz), 5.01 (1H, t, J=5.0 Hz), 5.45 (1H, s), 6.06 (1H, s). IR (Nujol): 3240, 1691, 1314, 1140 cm^{-1}. *Anal.* Calcd for $C_{27}H_{55}IN_4O_5S$: C, 48.06; H, 8.22; N, 8.30; S, 4.75. Found: C, 47.60; H, 8.13; N, 8.27; S, 4.75.

3-[2-(3-Methylureido)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]-propylquinolinium Iodide (33) Yield 80%. Yellow powder. mp 83—86 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=5.0 Hz), 1.25 (30H, s), 1.48 (2H, m), 2.61 (3H, d, J=4.0 Hz), 2.65 (2H, m), 3.08 (2H, m), 3.28 (2H, m), 3.54 (2H, m), 4.11 (3H), 5.40—5.70 (3H), 6.18 (1H, d, J=7.0 Hz), 6.30 (1H, br s), 8.01 (1H, t, J=7.0 Hz), 8.16 (1H, dd, J=5.0, 7.0 Hz), 8.25—8.45 (2H, m), 8.68 (1H, d, J=7.0 Hz), 8.99 (1H, d, J=7.0 Hz), 10.06 (1H, d, J=5.0 Hz). IR (Nujol): 3220, 1694, 1634, 1257, 1144 cm^{-1}. *Anal.* Calcd for $C_{36}H_{62}IN_5O_5S \cdot 0.5H_2O$: C, 53.19; H, 7.81; I, 15.61; N, 8.62; S, 3.94. Found: C, 53.09; H, 7.87; I, 15.24; N, 8.67; S, 4.24.

1-Dimethyl-*tert*-butylsilyloxy-3-trityloxypropan-2-ol (35) Yield 96%. Oil. NMR ($CDCl_3$) δ: 0.02 (3H, s), 0.03 (3H, s), 0.84 (9H, s), 2.46 (1H, d, J=5.0 Hz), 3.14 (1H, ABX, J=9.2, 5.8 Hz), 3.22 (1H, ABX, J=9.2, 5.8 Hz), 3.67 (1H, ABX, J=9.4, 4.9 Hz), 3.70 (1H, ABX, J=9.4, 3.1 Hz), 3.75—3.90 (1H, m), 7.10—7.50 (15H, m). IR ($CHCl_3$): 3680, 3580 cm^{-1}.

1-Dimethyl-*tert*-butylsilyloxy-2-(5-methyl-1*H*-tetrazol-1-yl)-3-trityloxypropane (36a) and 1-Dimethyl-*tert*-butylsilyloxy-2-(5-methyl-2*H*-tetrazol-2-yl)-3-trityloxypropane (37a) To a stirred solution of **35** (1.0 g, 2.23 mmol), PPh_3 (885 mg, 3.38 mmol) and 5-methyltetrazol (281 mg, 3.35 mmol) in THF (50 ml) was added DEAD (0.53 ml, 3.38 mmol) at 0 °C, and the mixture was stirred at room temperature overnight. The solvent was removed and the crude residue was purified by silica gel column chromatography using toluene as an eluent, and **36a** and **37a** were obtained. **36a**: yield 31%. Oil. NMR ($CDCl_3$) δ: −0.16 (3H, s), −0.09 (3H, s), 0.73 (9H, s), 2.56 (3H, s), 3.55 (1H, ABX, J=9.8, 5.6 Hz), 3.67 (1H, ABX, J=9.8, 9.4 Hz), 3.91 (1H, ABX, J=10.4, 9.9 Hz), 3.97 (1H, ABX, J=10.4,

5.9 Hz), 4.35—4.50 (1H, m), 7.15—7.40 (15H, m). **37a**: yield 64%. Oil. NMR ($CDCl_3$) δ: −0.10 (3H, s), −0.08 (3H, s), 0.74 (9H, s), 2.54 (3H, s), 3.57 (1H, ABX, J=9.8, 4.6 Hz), 3.36 (1H, ABX, J=9.8, 7.6 Hz), 4.0—4.15 (2H, m), 4.95—5.15 (1H, m), 7.10—7.35 (15H, m).

2-(5-Methyl-1*H*-tetrazol-1-yl)-1-trityloxypropan-3-ol (38a) Yield 91%. Colorless powder. mp 148—150 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 2.49 (3H, s), 3.50—3.65 (3H, m), 3.90—4.20 (2H, m), 4.35—4.50 (1H, m), 7.10—7.35 (15H, m). IR ($CHCl_3$): 3350 cm^{-1}. *Anal.* Calcd for $C_{24}H_{24}N_4O_2 \cdot 0.1H_2O$: C, 71.66; H, 6.06; N, 13.93. Found: C, 71.48; H, 6.04; N, 13.93.

2-(5-Methyl-1*H*-tetrazol-1-yl)-1-octadecylcarbamoyloxypropan-3-ol (39a) Yield 49%. Colorless powder. mp 80—83 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.54 (3H, s), 3.13 (2H, q, J=6.4 Hz), 4.00—4.25 (2H, m), 4.38 (1H, ABX, J=11.8, 8.3 Hz), 4.56 (1H, ABX, J=11.8, 4.5 Hz), 4.65—4.80 (1H, m), 5.01 (1H, t, J=5.8 Hz). IR ($CHCl_3$): 3450, 1730 cm^{-1}. *Anal.* Calcd for $C_{24}H_{47}N_5O_3$: C, 63.54; H, 10.44; N, 15.44. Found: C, 63.06; H, 10.37; N, 15.36.

3-Amino-2-(5-methyl-1*H*-tetrazol-1-yl)-1-octadecylcarbamoyloxypropane (41a) To a stirred solution of **39a** (1.02 g, 2.25 mmol), PPh_3 (885 mg, 3.38 mmol) and HN_3 (1.8 M/l benzene solution) (1.9 ml, 3.38 mmol) in THF (50 ml) was added DEAD (0.53 ml, 3.38 mmol) at −50 °C, and the mixture was stirred at 0 °C for 2 h. 10% Pd–C (150 mg) was added to the mixture and hydrogenated at 1 atm for 30 min. After removal of the catalyst by passing it through a pad of Celite, the solvent was removed and the crude residue was purified by silica gel column chromatography using a $CHCl_3$–MeOH (9 : 1) mixture as an eluent. **41a** was obtained as an oil. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7 Hz), 2.52 (3H, s), 3.13 (2H, q, J=6.6 Hz), 3.15—3.45 (2H, m), 4.23 (1H, ABX, J=12.6, 9.8 Hz), 4.52 (1H, ABX, J=12.6, 4.2 Hz), 4.50—4.65 (1H, m), 5.07 (1H, t, J=6.0 Hz).

3-(3-Chloropropylsulfonylamino)-2-(5-methyl-1*H*-tetrzol-1-yl)-1-octadecylcarbamoyloxypropane (42a) Yield 80%. Colorless powder. mp 74—77 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.5 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.15—2.35 (2H, m), 2.57 (3H, s), 3.12 (2H, q, J=6.8 Hz), 3.23 (2H, t, J=7.0 Hz), 3.67 (2H, t, J=6.2 Hz), 3.74 (2H, t, J=7.0 Hz), 4.35 (1H, ABX, J=11.8, 7.5 Hz), 4.50 (1H, ABX, J=11.8, 4.5 Hz), 4.75—5.0 (1H, m), 5.01 (1H, t, J=6.0 Hz), 6.22 (1H, t, J=7.0 Hz). IR ($CHCl_3$): 1732, 1345 cm^{-1}. *Anal.* Calcd for $C_{27}H_{53}ClN_6O_4S$: C, 54.66; H, 9.00; Cl, 5.98; N, 14.17; S, 5.40. Found: C, 54.28; H, 8.94; Cl, 6.10; N, 14.36; S, 5.30.

3-(3-Iodopropylsulfonylamino)-2-(5-methyl-1*H*-tetrazol-1-yl)-1-octadecylcarbamoyloxypropane (43a) Yield 94%. Colorless powder. mp 82.5—83.5 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=9.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.15—2.35 (2H, m), 2.58 (3H, s), 3.05—3.25 (4H, m), 3.29 (3H, t, J=7.0 Hz), 3.74 (2H, t, J=6.0 Hz), 4.35 (1H, ABX, J=1.0, 7.7 Hz), 4.51 (1H, ABX, J=11.0, 5.3 Hz), 4.75—4.95 (1H, m), 5.02 (1H, t, J=6.0 Hz), 6.26 (1H, t, J=6.0 Hz). IR ($CHCl_3$): 1728, 1338 cm^{-1}. *Anal.* Calcd for $C_{27}H_{53}IN_6O_4S$: C, 47.36; H, 7.80; I, 18.53; N, 12.27; S, 4.68. Found: C, 47.16; H, 7.61; I, 18.73; N, 12.24; S, 4.91.

3-[2-(5-Methyl-1*H*-tetrazol-1-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (44) Yield 86%. Yellow powder. mp 77—87 °C. NMR ($CDCl_3$) δ: 0.90 (3H, t, J=6.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.40—2.75 (2H, m), 2.58 (3H, s), 2.95—3.15 (2H, m), 3.40—3.80 (2H, m), 3.60—3.95 (2H, m), 4.25—4.60 (2H, m), 4.85—5.10 (1H, m), 5.25—5.55 (3H, m), 6.90—7.15 (1H, m), 7.94 (1H, t, J=7.6 Hz), 8.10—8.40 (3H, m), 8.68 (1H, d, J=9.0 Hz), 9.05 (1H, d, J=8.4 Hz), 9.85 (1H, d, J=5.8 Hz). IR ($CHCl_3$): 1729, 1334 cm^{-1}. *Anal.* Calcd for $C_{36}H_{60}IN_7O_4S$: C, 53.13; H, 7.43; I, 15.59; N, 12.05; S, 3.94. Found: C, 52.94; H, 7.44; I, 15.81; N, 12.05; S, 4.02.

2-(5-Methyl-2*H*-tetrazol-2-yl)-1-trityloxypropan-3-ol (46a) Yield 96%. Colorless powder. mp 126—127 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 2.49 (3H, s), 2.94 (1H, t, J=6.5 Hz), 3.60—3.75 (2H, m), 3.95—4.30 (2H, m), 4.90—5.10 (1H, m), 7.15—7.45 (15H, m). IR ($CHCl_3$): 3400 cm^{-1}. *Anal.* Calcd for $C_{24}H_{24}N_4O_2 \cdot 0.5H_2O$: C, 70.40; H, 6.15; N, 13.68. Found: C, 70.73; H, 5.97; N, 13.66.

2-(5-Methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropan-3-ol (47a) Yield 52%. Colorless powder. mp 76—77 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0 Hz), 1.25 (30H, s), 1.35—1.55 (2H, m), 2.54 (3H, s), 3.14 (2H, q, J=6.5 Hz), 4.14 (2H, d, J=5.8 Hz), 4.55—4.70 (2H, m), 4.80—4.95 (1H, m), 5.00—5.20 (1H, m). IR ($CHCl_3$): 3440, 1722 cm^{-1}. *Anal.* Calcd for $C_{24}H_{47}N_5O_3$: C, 63.54; H, 10.44; N, 15.44. Found: C, 63.36; H, 10.46; N, 15.32.

3-Amino-2-(5-methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropane (49a) Yield 95%. Crude. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.5 Hz), 1.25 (30H, s), 1.40—1.65 (2H, m), 2.55 (3H, s), 3.12 (2H, q, J=6.6 Hz), 3.25—3.35 (2H, m), 4.47 (1H, ABX, J=11.6, 8.0 Hz), 4.59 (1H, ABX, J=11.6, 4.1 Hz), 4.80—4.95 (1H, m), 4.95—5.10 (1H, m).

3-(3-Chloropropylsulfonylamino)-2-(5-methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropane (50a) Yield 63%. Colorless powder. mp 70—70.5 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0 Hz), 1.25 (30H, s), 1.40—1.65 (2H, m), 2.15—2.35 (2H, m), 2.55 (3H, s), 3.05—3.25 (4H, m), 3.66 (2H, t, J=6.0 Hz), 3.70—3.90 (2H, m), 4.56 (2H, d, J=5.6 Hz), 4.92 (1H, t, J=6.0 Hz), 5.10—5.30 (1H, m), 5.64 (1H, t, J=6.0 Hz). *Anal.* Calcd for $C_{27}H_{53}ClN_6O_4S$: C, 54.66; H, 9.00; Cl, 5.98; N, 14.17; S, 5.40. Found: C, 54.66; H, 8.94; Cl, 6.05; N, 14.14; S, 5.49.

3-(3-Iodopropylsulfonylamino)-2-(5-methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropane (51a) Yield 92%. Colorless powder. mp 53.5—54 °C (from CH_2Cl_2–MeOH). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.26 (2H, q, J=6.0 Hz), 3.05—3.20 (4H, m), 3.27 (2H, t, J=6.7 Hz), 3.73 (1H, ABX, J=15.4, 5.7 Hz), 3.85 (1H, ABX, J=15.4, 7.3 Hz), 4.56 (2H, d, J=5.4 Hz), 4.91 (1H, t, J=6.0 Hz), 5.10—5.30 (1H, m), 5.60 (1H, t, J=6.0 Hz). IR ($CHCl_3$): 1722, 1340 cm^{-1}.

3-[2-(5-Methyl-2*H*-tetrazol-2-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (52) Yield 74%. Yellow amorphous powder. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.40—1.60 (2H, m), 2.46 (3H, s), 2.45—2.8 (2H, m), 2.95—3.20 (2H, m), 3.50—3.75 (2H, m), 3.65—3.95 (2H, m), 4.35—4.70 (2H, m), 5.15—5.45 (2H, m), 5.35—5.70 (2H, m), 6.70—6.95 (1H, m), 7.99 (1H, t, J=8.0 Hz), 8.10—8.40 (3H, m), 8.70 (1H, d, J=9.4 Hz), 9.04 (1H, d, J=8.2 Hz), 10.04 (1H, d, J=5.6 Hz). IR ($CHCl_3$): 1726, 1340 cm^{-1}. *Anal.* Calcd for $C_{36}H_{60}IN_7O_4S \cdot 0.5H_2O$: C, 52.54; H, 7.47; I, 15.42; N, 11.92; S, 3.90. Found: C, 52.39; H, 7.51; I, 15.62; N, 12.04; S, 3.42.

2-(3-Methyl-2*H*-1,2,4-triazol-2-yl)-1-trityloxypropan-3-ol (38b) and 2-(3-Methyl-1*H*-1,2,4-triazol-1-yl)-1-trityloxypropan-3-ol (46b) Compounds **36b** and **37b** were prepared from **35** by the same procedure used to prepare **36a** and **37a**. They were separated after deprotection of their *tert*-butyldimethylsilyl (TBDMS) groups. **38b**: yield 42%. Colorless powder. NMR ($CDCl_3$) δ: 2.46 (3H, s), 3.40—3.70 (3H, m), 3.85—4.05 (2H, m), 4.25—4.40 (1H, m), 7.15—7.40 (15H, m), 7.75 (1H, s). **46b**: yield 43%. Colorless powder. NMR ($CDCl_3$) δ: 2.38 (3H, s), 3.42—3.63 (2H, m), 3.96 (2H, d, J=4.6 Hz), 4.20—4.34 (1H, m), 7.20—7.35 (15H, m), 8.30 (1H, s). IR ($CHCl_3$): 3380 cm^{-1}.

2-(3-Methyl-2*H*-1,2,4-triazol-2-yl)-1-octadecylcarbamoyloxypropan-3-ol (39b) Yield 72%. Colorless powder. mp 72—73 °C. NMR ($CDCl_3$) δ: 0.85 (3H, t, J=6.4 Hz), 1.23 (30H, s), 1.35—1.60 (2H, m), 2.40 (3H, s), 3.05—3.20 (2H, m), 3.90—4.10 (2H, m), 4.20—4.60 (4H, m), 4.97 (1H, t, J=6.0 Hz), 7.74 (1H, s). IR ($CHCl_3$): 3450, 2920, 2850, 1720, 1510, 1230 cm^{-1}.

3-Amino-2-(3-Methyl-2*H*-1,2,4-triazol-2-yl)-1-octadecylcarbamoyloxypropane (41b) Yield 52%. Crude. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.35—1.60 (2H, m), 2.47 (3H, s), 3.05—3.40 (4H, m), 4.15—4.60 (3H, m), 4.75—4.90 (1H, br), 7.85 (1H, s). IR ($CHCl_3$): 3450, 2930, 2850, 1725, 1520, 1240 cm^{-1}.

3-(3-Chloropropylsulfonylamino)-2-(3-methyl-2*H*-1,2,4-triazol-2-yl)-1-octadecylcarbamoyloxypropane (42b) Yield 90%. Amorphous powder. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.35—1.60 (2H, m), 2.25—2.35 (2H, m), 2.46 (3H, s), 3.05—3.25 (4H, m), 3.55—3.62 (4H, m), 4.20—4.50 (2H, m), 4.60—4.80 (1H, m), 5.01 (1H, t, J=5.6 Hz), 6.44 (1H, t, J=7.0 Hz), 7.71 (1H, s). IR ($CHCl_3$): 3450, 2930, 1725, 1510, 1335, 1220, 1150 cm^{-1}.

3-(3-Iodopropylsulfonylamino)-2-(3-methyl-2*H*-1,2,4-triazol-2-yl)-1-octadecylcarbamoyloxypropane (43b) Yield 64%. Pale yellow powder. mp 102—105 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.35—1.60 (2H, m), 2.20—2.40 (2H, m), 2.47 (3H, s), 3.05—3.25 (3H, m), 3.28 (2H, t, J=6.6 Hz), 3.55—3.70 (2H, m), 4.20—4.50 (2H, m), 4.60—4.80 (1H, m), 4.85—5.00 (1H, m), 6.10—6.40 (1H, br), 7.74 (1H, s). *Anal.* Calcd for $C_{28}H_{54}IN_5O_4S \cdot 0.5H_2O$: C, 48.55; H, 8.00; I, 18.32; N, 10.11; S, 4.63. Found: C, 48.20; H, 7.70; I, not done; N, 10.09; S, 4.81.

3-[2-(3-Methyl-2*H*-1,2,4-triazol-2-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (45) Yield 76%. Yellow amorphous powder. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.35—1.60 (2H, m), 2.49 (3H, s), 2.45—2.70 (2H, m), 2.90—3.20 (2H, m), 3.40—3.80 (4H, m), 4.15—4.55 (2H, m), 4.70—4.90 (1H, m), 5.35—5.60 (3H, m), 6.90—7.10 (1H, m), 7.71 (1H, s), 7.97 (1H, d, J=7.7 Hz), 8.10—8.30 (1H, m), 8.29 (1H, d, J=8.0 Hz), 8.67 (1H, d, J=9.2 Hz), 9.03 (1H, d, J=9.6 Hz), 10.07 (1H, d, J=6.4 Hz). IR ($CHCl_3$): 1719, 1330 cm^{-1}.

2-(3-Methyl-1*H*-1,2,4-triazol-1-yl)-1-octadecylcarbamoyloxypropan-3-ol (47b) Yield 79%. Colorless powder. mp 74—77 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.37—1.58 (2H, m), 2.42 (3H, s), 3.07—3.23 (2H, m), 4.00 (2H, d, J=3.8 Hz), 4.31—4.62 (3H, m), 4.72—4.88

(1H, m), 8.18 (1H, s). IR ($CHCl_3$): 3438, 1714 cm^{-1}. *Anal.* Calcd for $C_{25}H_{48}N_4O_3 \cdot 0.1H_2O$: C, 66.07; H, 10.69; N, 12.33. Found: C, 65.90; H, 10.61; N, 12.55.

3-Amino-2-(3-Methyl-1*H*-1,2,4-triazol-1-yl)-1-octadecylcarbamoyloxypropane (49b) Yield 32%. Amorphous powder. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.31—1.56 (2H, m), 1.92 (2H, br s), 2.40 (3H, s), 2.90—3.35 (4H, m), 4.23—5.53 (3H, m), 4.70—4.87 (1H, m), 8.03 (1H, s). IR ($CHCl_3$): 3440, 1715 cm^{-1}.

3-(3-Chloropropylsulfonylamino)-2-(3-methyl-1*H*-1,2,4-triazol-1-yl)-1-octadecylcarbamoyloxypropane (50b) Yield 73%. Colorless powder. mp 88—89 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.38—1.53 (2H, m), 2.17—2.34 (2H, m), 2.38 (3H, s), 3.06—3.25 (4H, m), 3.52—3.76 (4H, m), 4.26—4.50 (2H, m), 4.57—4.75 (1H, m), 4.76—4.89 (1H, m), 5.70—5.80 (1H, m), 8.08 (1H, s). IR ($CHCl_3$): 1717, 1330, 1144 cm^{-1}. *Anal.* Calcd for $C_{28}H_{54}ClN_5O_4S \cdot 0.2H_2O$: C, 56.44; H, 9.20; Cl, 5.95; N, 11.75; S, 5.38. Found: C, 56.22; H, 9.13; Cl, 5.89; N, 11.76; S, 5.52.

3-(3-Iodopropylsulfonylamino)-2-(3-methyl-1*H*-1,2,4-triazol-1-yl)-1-octadecylcarbamoyloxypropane (51b) Yield 80%. Pale yellow powder. mp 82—85 °C. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 2.20—2.38 (2H, m), 2.39 (3H, s), 3.06—3.20 (4H, m), 3.28 (2H, t, J=6.6 Hz), 3.48—3.75 (2H, m), 4.28—4.49 (2H, m), 4.58—4.73 (1H, m), 4.79—4.90 (1H, m), 5.71—5.86 (1H, m), 8.11 (1H, s). IR ($CHCl_3$): 1717, 1328, 1141 cm^{-1}. *Anal.* Calcd for $C_{28}H_{54}IN_5O_4S \cdot 0.2H_2O$: C, 48.93; H, 7.98; I, 18.46; N, 10.19; S, 4.66. Found: C, 48.60; H, 7.86; I, 18.51; N, 10.06; S, 4.68.

3-[2-(3-Methyl-1*H*-1,2,4-triazol-1-yl)-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (53) Yield 95%. Yellow amorphous powder NMR. ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.25 (30H, s), 1.35—1.60 (2H, m), 2.28 (3H, s), 2.46—2.84 (2H, m), 2.97—3.20 (2H, m), 3.33—3.79 (4H, m), 4.24—4.49 (2H, m), 4.72—4.94 (1H, m), 5.34—5.60 (3H, m), 6.90—7.09 (1H, m), 7.97 (1H, t, J=7.6 Hz), 8.11—8.40 (4H, m), 8.67 (1H, d, J=9.0 Hz), 8.99 (1H, d, J=8.6 Hz), 10.16 (1H, d, J=5.0 Hz). IR ($CHCl_3$): 1718, 1320, 1140 cm^{-1}.

(*S*)- and (*R*)-4-(3-Chloropropylsulfonyl)benzyloxyaminomethyl-2,2-dimethyl-1,3-dioxolane (57) To an ice-cooled and stirred solution of (*S*)-2,2-dimethyl-1,3-dioxolane-4-methanol (**4**) (1.88 g, 1.42 mmol), PPh_3 (4.85 g, 1.85 mmol), and *N*-benzyloxy-3-chloropropanesulfonamide (**56**) (5.4 g, 1.85 mmol) in THF (150 ml) was added DEAD (2.91 ml, 1.85 mmol), and the mixture was stirred at room temperature overnight. After removal of the solvent, the crude product was purified by silica gel column chromatography using an AcOEt–hexane (1 : 4) mixture as an eluent, and (*S*)-**57** (5.34 g, 93%) was obtained as an oil. NMR ($CDCl_3$) δ: 1.32 (3H, s), 1.41 (3H, s), 2.24—2.38 (2H, m), 3.60—3.81 (6H, m), 3.94—4.08 (2H, m), 4.26—4.38 (1H, m), 5.29 (2H, s), 7.30—7.45 (5H, m). IR ($CHCl_3$): 2960, 1725, 1440, 1380, 1355, 1310, 1230, 1160, 1080 cm^{-1}. (*R*)-**57** was obtained in a similar manner.

(*S*)- and (*R*)-3-(3-Chloropropylsulfonylamino)propane-1,2-diol (58) To an ice-cooled and stirred solution of (*S*)-**57** (6.94 g, 17.1 mmol) in the mixture of THF (60 ml) and MeOH (12 ml) was added 1 N HCl (3 ml), and the mixture was stirred at room temperature overnight. The product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The crude product and 5% Pd–C were added to the mixture of THF (25 ml) and AcOH (25 ml), which was then hydrogenated at 1 atm for 5 h. After removal of the catalyst, the organic layer was concentrated *in vacuo*, and (*S*)-(−)-**58** (3.27 g, 83%) was obtained on recrystallization from AcOEt–hexane as colorless prisms. mp 75—76.5 °C. $[\alpha]_D^{23.5}$ −12.1±0.5° (c=1.01, MeOH). NMR ($CDCl_3$) δ: 2.21—2.35 (2H, m), 3.08—3.30 (4H, m), 3.52—3.82 (3H, m), 3.69 (2H, t, J=6.2 Hz). IR ($CHCl_3$): 3650, 3525, 1310, 1140 cm^{-1}. *Anal.* Calcd for $C_6H_{14}ClNO_4S$: C, 31.10; H, 6.09; Cl, 13.84; N, 6.05; S, 15.30. Found: C, 30.92; H, 6.04; Cl, 13.79; N, 6.32; S, 15.28.

(*R*)-(+)-**58** was obtained in a similar manner. Colorless prisms. mp 75—76.5 °C. $[\alpha]_D^{23.5}$ +10.0±0.5° (c=1, MeOH). *Anal.* Calcd for $C_6H_{14}ClNO_4S$: C, 31.10; H, 6.09; Cl, 13.84; N, 6.05; S, 15.30. Found: C, 30.95; H, 6.00; Cl, 13.81; N, 6.26; S, 15.31.

(*S*)- and (*R*)-3-(3-Chloropropylsulfonylamino)-1-octadecylcarbamoyloxypropan-2-ol (59) To a solution of (*S*)-(−)-**58** (1.39 g, 6.0 mmol) in a mixture of pyridine (10 ml) and CH_2Cl_2 (50 ml) were added octadecyl isocyanate (1.95 g, 6.6 mmol) and a catalytic amount of DMAP, and the mixture was stirred at room temperature overnight. After removal of the solvent, the crude product was purified by silica gel column chromatography using a $CHCl_3$–MeOH (40 : 1) mixture as an eluent, and (*S*)-(−)-**59** (1.76 g, 54%) was obtained on reprecipitation from dichloroethane ($ClCH_2CH_2Cl$) as a colorless powder. mp 94—95 °C. $[\alpha]_D^{24}$ −11.0±0.5° (c=1.01, $CHCl_3$). NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.4 Hz), 1.26 (30H, s), 1.40—1.60 (2H, m), 2.20—2.38 (2H, m), 3.05—3.30 (6H, m), 3.69 (2H, t, J=6.1 Hz), 3.84—3.98 (1H, m). IR ($CHCl_3$): 3380, 2930, 2850, 1710, 1520, 1450, 1330, 1150 cm^{-1}. *Anal.* Calcd for $C_{25}H_{51}ClN_2O_5S$: C, 56.96; H, 9.75; Cl, 6.72; N, 5.31; S, 6.08. Found: C, 56.66; H, 9.70; Cl, 6.89; N, 5.32; S, 6.06. (*R*)-(+)-**59** was obtained in a similar manner. Colorless powder. mp 94—95 °C. $[\alpha]_D^{24}$ +8.8±0.5° (c=1, $CHCl_3$). *Anal.* Calcd for $C_{25}H_{51}ClN_2O_5S$: C, 56.96; H, 9.75; Cl, 6.72; N, 5.31; S, 6.08. Found: C, 57.16; H, 9.76; Cl, 6.75; N, 5.30; S, 5.92. Racemic **59**: mp 91.5—93.5 °C (from AcOEt).

(*S*)- and (*R*)-3-(3-Chloropropylsulfonylamino)-2-methoxy-1-octadecylcarbamoyloxypropane (60) To a solution of (*S*)-(−)-**59** (1.58 g, 3.0 mmol) in CH_2Cl_2 (30 ml) was added $(CH_3)_3O^+BF_4^-$ (666 mg, 4.5 mmol), and the mixture was refluxed for 2 h. $(CH_3)_3O^+BF_4^-$ (340 mg, 2.3 mmol) was added to the mixture, and the mixture was further refluxed for 1 h. The product was isolated by CH_2Cl_2 extraction. The CH_2Cl_2 layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using a $CHCl_3$–MeOH (30 : 1) mixture as an eluent. (*S*)-(−)-**60** (700 mg, 43%) was obtained as a colorless powder and (*S*)-(−)-**59** (780 mg, 49%) was recovered, mp 73—74 °C [from isopropyl ether (iso-Pr_2O)]. $[\alpha]_D^{24}$ −9.1±0.5° (c=1.01, $CHCl_3$). *Anal.* Calcd for $C_{26}H_{53}ClN_2O_5S$: C, 57.70; H, 9.87; Cl, 6.55; N, 5.18; S, 5.92. Found: C, 57.48; H, 9.78; Cl, 6.38; N, 5.40; S, 5.93.

(*R*)-(+)-**60** was obtained in a similar manner. Colorless powder. mp 73—74 °C (from iso-Pr_2O). $[\alpha]_D^{24}$ +9.0±0.5° (c=1, $CHCl_3$). *Anal.* Calcd for $C_{26}H_{53}ClN_2O_5S$: C, 57.70; H, 9.87; Cl, 6.55; N, 5.18; S, 5.92. Found: C, 57.47; H, 9.84; Cl, 6.34; N, 5.44; S, 5.90. Racemic **60**: mp 64.5—66 °C (from $CHCl_3$–hexane).

(*S*)- and (*R*)-3-(3-Iodopropylsulfonylamino)-2-methoxy-1-octadecylcarbamoyloxypropane (61) (*S*)-(−)-**61**: Colorless powder. mp 74—75 °C (from iso-Pr_2O). $[\alpha]_D^{24}$ −7.8±0.5° (c=1.01, $CHCl_3$). *Anal.* Calcd for $C_{26}H_{53}IN_2O_5S$: C, 49.12; H, 8.44; I, 20.08; N, 4.56; S, 5.34. Found: C, 49.24; H, 8.36; I, 19.98; N, 4.64; S, 5.34.

(*R*)-(+)-**61**: Colorless powder. mp 74—75 °C (from iso-Pr_2O). $[\alpha]_D^{24}$ +7.9±0.5° (c=1.01, $CHCl_3$). *Anal.* Calcd for $C_{26}H_{53}IN_2O_5S$: C, 49.12; H, 8.44; I, 20.08; N, 4.56; S, 5.34. Found: C, 49.41; H, 8.42; N, 4.70; S, 5.32; I, 19.79. Racemic **61**: mp 61.5—62.5 °C (from $CHCl_3$–hexane).

(*S*)- and (*R*)-3-[2-Methoxy-3-(octadecylcarbamoyloxy)propylaminosulfonyl]propylquinolinium Iodide (3) (*S*)-(−)-**3**: Yellow powder. mp 57—59 °C (from Et_2O–CH_2Cl_2). $[\alpha]_D^{24.5}$ −2.8±0.4° (c=1, $CHCl_3$). *Anal.* Calcd for $C_{35}H_{60}IN_3O_5S \cdot 0.5H_2O$: C, 54.54; H, 7.98; I, 16.46; N, 5.45; S, 4.16. Found: C, 54.49; H, 7.94; I, 16.55; N, 5.72; S, 4.50.

(*R*)-(+)-**3**: Yellow powder. mp 57—59 °C (from Et_2O–CH_2Cl_2). $[\alpha]_D^{24.5}$ +2.0±0.4° (c=1, $CHCl_3$). *Anal.* Calcd for $C_{35}H_{60}IN_3O_5S \cdot 0.6H_2O$: C, 54.41; H, 7.98; I, 16.42; N, 5.44; S, 4.15. Found: C, 54.10; H, 7.87; I, 16.60; N, 5.66; S, 4.52. Racemic **3**: mp 55—57 °C (from Et_2O–CH_2Cl_2).

(*R*)- and (*S*)-1-Octadecylcarbamoyloxypropane-2,3-diol (5) (*R*)-(+)-**5**: Colorless powder. mp 95—96 °C (from AcOEt). $[\alpha]_D^{25}$ +0.7±0.4° (c=1.02, THF). *Anal.* Calcd for $C_{22}H_{45}O_4N$: C, 68.17; H, 11.70; N, 3.61. Found: C, 68.04; H, 11.68; N, 3.69.

(*S*)-(−)-**5**: Colorless powder. mp 94.5—95.5 °C (from AcOEt). $[\alpha]_D^{24}$ −2.3±0.4° (c=1.02, THF). *Anal.* Calcd for $C_{22}H_{45}NO_4$: C, 68.17; H, 11.70; N, 3.61. Found: C, 68.06; H, 11.68; N, 3.68.

(*S*)- and (*R*)-2-(5-Methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxy-3-propanol (47a) (*S*)-(+)-**47a**: Colorless powder. mp 77—79 °C (from iso-Pr_2O). $[\alpha]_D^{25.5}$ +8.1±0.5° (c=1, $CHCl_3$). *Anal.* Calcd for $C_{24}H_{47}N_5O_3$: C, 63.54; H, 10.44; N, 15.44. Found: C, 63.27; H, 10.36; N, 15.58.

(*R*)-(−)-**47a**: Colorless powder. mp 76—78 °C (from iso-Pr_2O). $[\alpha]_D^{23}$ −8.4±0.5° (c=1.02, $CHCl_3$). *Anal.* Calcd for $C_{24}H_{47}N_5O_3$: C, 63.54; H, 10.44; N, 15.44. Found: C, 63.33; H, 10.33; N, 15.43. Racemic **47a**: mp 76—77 °C (from CH_2Cl_2–MeOH).

(*S*)- and (*R*)-3-(*N*-Benzyloxy-3-chloropropylsulfonylamino)-2-(5-methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropane (54a) To an ice-cooled and stirred solution of (*S*)-(−)-**47a** (528 mg, 1.16 mmol), PPh_3 (397 mg, 1.51 mmol) and $PhCH_2OCONHSO_2(CH_2)_3Cl$ (441 mg, 1.51 mmol) in benzene (20 ml) was added DEAD (0.238 ml, 1.51 mmol), and the mixture was stirred at room temperature overnight. After removal of the solvent, the crude product was purified by silica gel column chromatography using an AcOEt–hexane (1 : 3) mixture as an eluent, and (*S*)-(−)-**54a** (668 mg, 79%) was obtained as a colorless powder. NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.5 Hz), 1.25 (30H, s), 1.35—1.55 (2H, m), 2.15—2.29 (2H, m), 2.49 (3H, s), 3.05—3.20 (2H, m), 3.42—3.73 (4H, m), 4.16—4.37 (2H, m), 4.45—4.70 (3H, m), 5.14, 5.23 (2H, ABq, J=14.4 Hz), 5.30—5.45 (1H, m), 7.30—7.50 (5H, m). (*S*)-(−)-**54a**: mp 72—74 °C (from

hexane). $[\alpha]_D^{23}$ $-12.8\pm0.5°$ ($c=1.01$, $CHCl_3$). *Anal.* Calcd for $C_{35}H_{59}ClN_6O_6S$: C, 57.79; H, 8.18; Cl, 4.87; N, 11.55; S, 4.41. Found: C, 57.75; H, 8.19; Cl, 4.66; N, 11.83; S, 4.43.

(*R*)-(+)-**54a** was obtained in a similar manner. Colorless powder. mp 72—74 °C (from hexane). $[\alpha]_D^{25.5}$ $+12.7\pm0.5°$ ($c=1.01$, $CHCl_3$). *Anal.* Calcd for $C_{35}H_{59}ClN_6O_6S$: C, 57.79; H, 8.18; Cl, 4.87; N, 11.55; S, 4.41. Found: C, 57.49; H, 8.15; Cl, 4.71; N, 11.77; S, 4.37.

(*S*)- and (*R*)-3-(3-Iodopropylsulfonylamino)-2-(5-methyl-2*H*-tetrazol-2-yl)-1-octadecylcarbamoyloxypropane (51a) To a solution of (*S*)-(−)-**54a** (578 mg, 0.795 mmol) in MEK (12 ml) was added NaI (1.2 g, 8.0 mmol), and the mixture was refluxed for 3 h. The mixture was cooled and poured into 0.5 N $Na_2S_2O_3$. The product was isolated by AcOEt extraction. The AcOEt layer was washed with saturated aqueous $NaHCO_3$ and saturated NaCl and then dried and evaporated. The product was purified by silica gel column chromatography using an AcOEt–hexane (2 : 3) mixture as an eluent, and (*S*)-(−)-**51a** (503 mg, 92%) was obtained on reprecipitation from iso-Pr_2O as a colorless powder. mp 59—61 °C. $[\alpha]_D^{25.5}$ $-8.5\pm0.5°$ ($c=1.01$, $CHCl_3$). *Anal.* Calcd for $C_{27}H_{53}IN_6O_4S$: C, 47.36; H, 7.80; I, 18.53; N, 12.27; S, 4.68. Found: C, 47.48; H, 7.77; I, 18.46; N, 12.40; S, 4.84.

(*R*)-(+)-**51a** was obtained in a similar manner. Colorless powder. mp 59—61 °C. $[\alpha]_D^{24}$ $+8.1\pm0.5°$ ($c=1.01$, $CHCl_3$). *Anal.* Calcd for $C_{27}H_{53}IN_6O_4S$: C, 47.36; H, 7.80; I, 18.53; N, 12.27; S, 4.68. Found: C, 47.19; H, 7.68; I, 18.39; N, 12.34; S, 4.57. Racemic **51a**: mp 53.5—54 °C (from CH_2Cl_2–MeOH).

(*R*)- and (*S*)-3-[2-(5-Methyl-2*H*-tetrazol-2-yl)-3-(octadecylcarbamoyloxy)pyropylaminosulfonyl]propylquinolinium Iodide (52) (*S*)-(−)-**52**: Yellow powder. mp 110—113 °C (from Et_2O–CH_2Cl_2). $[\alpha]_D^{25.5}$ $-2.7\pm0.4°$ ($c=1$, $CHCl_3$). *Anal.* Calcd for $C_{36}H_{60}IN_7O_4S\cdot0.5H_2O$: C, 52.54; H, 7.47; I, 15.42; N, 11.92; S, 3.90. Found: C, 52.55; H, 7.27; I, 15.59; N, 12.10; S, 4.07.

(*R*)-(+)-**52**: Yellow powder. mp 111—113 °C (from Et_2O–CH_2Cl_2). $[\alpha]_D^{24}$ $+2.2\pm0.4°$ ($c=1$, $CHCl_3$). *Anal.* Calcd for $C_{36}H_{60}IN_7O_4S\cdot0.5H_2O$: C, 52.54; H, 7.47; I, 15.42; N, 11.92; S, 3.90. Found: C, 52.62; H, 7.27; I, 15.46; N, 12.14; S, 4.19. Racemic **52**: Yellow amorphous powder.

Biological Methods Materials: C_{16}-PAF and CV-3988 were synthesized at Shionogi Research Laboratories, Osaka, Japan. Bovine serum albumin (BSA) was purchased from Sigma, St. Louis.

Inhibitory Effect on Rabbit Platelet-Rich Plasma (PRP) Aggregation: Preparation of Rabbit PRP Mature male rabbits (NIBS-JW) weighing 2.2—2.6 kg were used. With the animal under sodium pentobarbital anesthesia (Somnopentyl, Pitman Moore, *ca.* 20 mg/kg, i.v.), blood was withdrawn from the carotid artery through a cannulation tube using a syringe containing sodium citrate (3.8%, 1/10 volume). The blood was centrifuged at 200 *g* for 10 min at 22 °C to obtain PRP. The remaining blood was centrifuged at 3000 rpm for 10 min to obtain platelet-poor plasma (PPP).

Measurement of Inhibition of Platelet Aggregation Platelet aggregation was examined by the method of Born,[13] using an aggregometer (NKK Hema tracer 1, model: PAT-6A, Niko Bioscience Co., Ltd., Tokyo) as reported previously.[15] A pair of samples of PRP (230 μl) placed in a cuvette was warmed at 37 °C for 1 min with stirring (1100 rpm), and then a dimethyl sulfoxide (DMSO) solution of the test compound (1 μl) with saline (9 μl) was added. Exactly 2 min later, 10 μl of C_{16}-PAF (500 nM), which was dissolved in a saline solution containing 0.25% BSA, was added to each of the samples, and the changes in light transmission were recorded. The light transmission for PRP and PPP was taken as 0% and 100%, respectively, and the maximum light transmission after the addition of C_{16}-PAF as the maximum aggregation. The percent inhibition α was expressed as the difference between 1 and the ratio of the maximum aggregation with the test compound to that with the saline-DMSO.

The IC_{50} value for each compound was obtained by regression analysis of the concentration-inhibition relationship among 9—12 points of α covering 3—4 concentrations, and ranging from 10 to 100%, as obtained by three experiments.

Inhibitory Effect of C_{16}-PAF-Induced Lethality in Mice Male ddY (slc) mice, 4 to 5 weeks old, were used. Drugs or saline (control) were given i.v. (0.1 ml/10 g) through the tail vein 15 and 60 min before the injection of C_{16}-PAF. At given times, C_{16}-PAF (100 μg/kg) was given through the tail vein in a volume of 0.1 ml/10 g. Death was defined by the cessation of respiration. The survival rate was recorded 2 h after the injection of PAF.

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