RESEARCH ARTICLE

[View Article Online](#)
[View Journal](#) | [View Issue](#) Cite this: *Med. Chem. Commun.*,
2018, 9, 2106

Design, synthesis, and biological activity of novel ammonium salts containing sterically hindered phenolic fragment and phosphoryl group†

Ramilya R. Starodubtseva, ^a Elmira M. Gibadullina, ^{*a} Nurbala B. Pazilova, ^b
Anastasiia S. Sapunova, ^a Alexandra D. Voloshina, ^a Igor A. Sudakov, ^b
Alexandra B. Vyshtakalyuk, ^a Michael A. Pudovik,^a
Alexander R. Burilov ^a and Sergey V. Bukharov^b

Here, we present an approach to novel “hybrid” biologically active compounds based on a combination of sterically hindered phenol and ammonium pharmacophores in a single molecule. The novel target ammonium salts were obtained by the reaction of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-*N*-(2-(dimethylamino)alkyl)propanamide with aliphatic bromides or by the reaction of phosphorylated methyl-enequinones with diamines followed by alkylation with organic bromides. A series of twenty-three novel multifunctional ammonium salts that contain a sterically hindered phenolic fragment were assessed for antimicrobial, cytotoxic and antioxidant activity. The compounds exhibited antimicrobial activity against *Staphylococcus aureus* ATCC 209p, *Bacillus cereus* ATCC 8035, *Escherichia coli* CDC F-50, *Pseudomonas aeruginosa* ATCC 9027, *Aspergillus niger* BKM-1119, *Trichophyton mentagrophytes* var. *gypseum* 1773, and *Candida albicans* 855-653 in the concentration range of 442–0.70 μ M. The maximum activity of an ammonium salt among all the types of structure was observed in cases in which a decyl radical was present on the onium nitrogen atom. The most active compounds exhibited antioxidant activity at levels of 0.25 and 0.50 mM and did not display cytotoxic properties towards WI-38 (human embryonic lung cells) and Chang liver (human liver cells) cell lines in the concentration range of 0.70–11.3 μ M.

Received 25th September 2018,
Accepted 7th November 2018

DOI: 10.1039/c8md00481a

rsc.li/medchemcomm

1. Introduction

One modern trend in medicinal chemistry comprises the construction of multifunctional drugs. These compounds are characterized by a broad range of pharmacological effects and are capable of interacting with several targets. This becomes possible owing to the presence of several pharmacophore fragments, of which the effects are combined. These preparations possess more predictable pharmacokinetic profiles, and the risk of incompatibility with other preparations is reduced significantly owing to the decrease in the number of drugs prescribed to a patient.

We have chosen the onium fragment as a basic pharmacophore group. It is known that ammonium salts are of interest as physiologically active compounds.^{1,2} Onium structures are present in many natural and biologically im-

portant compounds (betaines, choline, and acetylcholine). The biomedical application of ammonium salts is based on the presence of local anesthetic, anti-inflammatory, and analgesic, as well as antifungal and antibacterial, activities, owing to their ability to be attracted to the negatively charged bacterial membrane;^{3–5} they are also able to inhibit human leukocyte elastase.⁶ Over the past two decades there have appeared a large number of reports on the bactericidal activity of ammonium salts against two main causative agents of sexually transmitted diseases, namely, *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.^{7–9} The exact mechanism of the effect of ammonium salts on bacteria was not studied; however, it is known that they neutralize the charge on membranes¹⁰ and dissolve bacterial membranes, whereupon a fatal leakage of the cell contents occurs through the opening.^{11,12}

The need to search for new antimicrobial drugs is justified, because microorganisms develop resistance to pharmaceutical drugs available on the market.¹³ The resistance of pathogenic bacteria to antibiotics has become a serious problem for the modern healthcare system and medicine in society and threatens the vital activities of mankind. The search for new agents to control resistant bacteria is one of the most important areas in the development of medicinal

^a Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, Arbuzov street 8, Kazan 420088, Russian Federation.E-mail: elmirak@iopc.ru^b Kazan National Research Technological University, Karl Marx street 68, Kazan 420015, Russian Federation

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c8md00481a

chemistry.¹⁴ It should be noted that many bactericidal quaternary ammonium salts are toxic, do not exhibit selectivity in high concentrations and destroy mammalian cell membranes.^{15,16}

A reduction in toxicity can be achieved by incorporating a sterically hindered phenolic fragment into the molecule.^{17,18} In addition, sterically hindered 2,6-dialkylphenols are biomimetics of the natural antioxidant α -tocopherol (vitamin E) and represent a class of known phenolic antioxidants. They are used to protect fuels, oils, polymeric materials, and food products from oxidative and thermal destruction; high-performance low-toxicity non-steroidal compounds that possess anti-inflammatory,^{19,20} antiviral,²¹ antiallergic,²² antimicrobial,²³ and UV-protecting activities²⁴ have been found among them.

Derivatives of 3-(3',5'-di-*tert*-butyl-4'-hydroxyphenyl)propionic acid (phenozan) (Fig. 1), also known as IKhFANs, are promising drugs for the therapy of Alzheimer's disease and other forms of dementia.²⁵ A choline fragment provides the anticholinesterase activity of the molecule, whereas a long-chain alkyl group enables penetration through the lipid bilayer of the cell membrane. The hydrophobicity of the substituents on the quaternary nitrogen atom in IKhFANs significantly affects their membranotropic characteristics. As the length of the aliphatic substituent and hence the hydrophobicity of the derivative increases, the echinocytogenic, stomatocytogenic, and hemolytic activities of IKhFANs first increase and then, after passing through a maximum, decrease.

IKhFANs that contain methyl groups on the nitrogen atom penetrate through the membrane to an insignificant extent and act less effectively in comparison with more hydrophobic homologs that contain octyl, decyl, and dodecyl groups.²⁶

In addition, an increase in antioxidant activity can also be achieved by the introduction of a phosphoryl group into the molecule together with a sterically hindered phenolic fragment. It is known that phosphorus-containing sterically hindered phenols exhibit antiperoxide activity together with anti-radical activity owing to the presence of a phosphoryl group.²⁷ A decrease in the promoting effects of mercury and tin compounds was shown during the long-term oxidation of lipids by peroxide in the presence of phosphoryl-containing sterically hindered phenols.²⁸ Functionalized phosphonates are effective inhibitors of various enzymes, including a series of proteases and esterases;²⁹ they are also used as haptens for the synthesis of catalytic antibodies that possess esterase activity.³⁰ In addition, aminophosphonates that contain a ste-

rically hindered phenolic fragment can be used for the prevention and treatment of degenerative joint diseases (osteoarthritis, cartilage loss after injury), abnormal smooth muscle cell proliferation, enhanced thrombosis and restenosis, as well as cardiovascular and neurological diseases.^{31,32}

Various procedures for the synthesis of aminophosphonates that contain a sterically hindered phenolic fragment are described in the literature.^{31–33} The main drawbacks of these approaches are the high temperatures of the reaction and the presence of catalysts, as well as the low yields of the products. A convenient approach for the synthesis of new derivatives of sterically hindered phenols that contain a phosphoryl fragment comprises the use of phosphorus-containing 2,6-di-*tert*-butyl-4-methylene-2,5-cyclohexadienones³⁴ in reactions with nucleophiles. Stable phosphorus-containing methylenequinones easily react with amines^{35–40} and aminoacetals^{41,42} to give the products of nucleophilic addition in high yields.

The strategy for the construction of “hybrid” ammonium compounds in this paper is based on a series of sequential transformations. In the first stage, structures are formed that contain a terminal dimethylamino group as a result of the reactions of phosphorylated methylenequinones or the methyl ester of 3,5-di-*tert*-butyl-4-hydroxyphenylpropionic acid with *N,N*-dimethylethane-1,2-diamine and *N,N*-dimethylpropane-1,3-diamine. In the second stage, the target hybrid ammonium structures are prepared as a result of the reaction of the terminal dimethylamino group with various organic bromides, such as aliphatic (ethyl, octyl, decyl, dodecyl, and hexadecyl) bromides and benzyl bromide, which differ in hydrophobicity. As a result of these transformations, the corresponding analogs of IKhFANs can be obtained, which contain an amine bond and an aminophosphonate group with a sterically hindered phenolic fragment. It is known that labile covalent bonds, such as ester bonds, are insufficiently stable in aqueous media over a broad range of pH values and biological media and are susceptible to gradual hydrolysis.⁴³ We expect that IKhFAN analogs that contain an amide bond, which is highly stable in biological media, can be of interest in terms of studying their antimicrobial activity.

In this paper, the structure–property relationship for a broad range of synthesized quaternary onium salts that contain a sterically hindered phenolic fragment and a phosphoryl group is analyzed. From this perspective, this study is accordingly divided into two parts. The first part is devoted to the synthesis of sterically hindered phenols that contain an onium fragment, whereas the second part is devoted to the preparation of their phosphorylated analogs.

2. Results and discussion

2.1 Chemistry

In the first stage, we modified methyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propanoate **1** with a dimethylalkanediamine fragment (Scheme 1) according to a previously described procedure.⁴⁴

Fig. 1 IKhFANs-10.

Scheme 1 Synthesis of amides 2 and 3.

The reaction of compounds 2 and 3 with ethyl, octyl, decyl, dodecyl, and hexadecyl bromides in a 1:1 ratio at room temperature in acetonitrile gave the ammonium salts 4a–e and 5a–e (Scheme 2).

In the second approach, aminophosphonates with a terminal tertiary amino group were prepared in the first step, which are of interest as by-products of the synthesis of ammonium salts. Previously, we developed a procedure for the synthesis of ammonium salts that was based on the reaction of diethyl [(3,5-di-tert-butyl-4-oxo-2,5-cyclohexadienylidene)-methyl]phosphonate with *N,N*-dimethylethane-1,2-diamine with the subsequent quaternization of the synthesized aminophosphonate.⁴⁵ In this work, ammonium salts based on methylenequinones 6b that contain a diisopropylphosphonate fragment were synthesized to determine the structure–property relationship. To increase the length of the spacer in the reactions with methylenequinones 6a and b, *N,N*-dimethylpropane-1,3-diamine was used.

The reactions of methylenequinones 6a and b with *N,N*-dimethylethane-1,2-diamine and *N,N*-dimethylpropane-1,3-diamine occur at room temperature to give the products of nucleophilic 1,6-addition 7a and b and 8a and b in high yields (Scheme 3).

The quaternization reactions of aminophosphonates 7a and b and 8a and b with ethyl, decyl and dodecyl bromides, as well as benzyl bromide, were carried out at room temperature to give products 9a and 9b– 16a and 16b in high yields (Scheme 4). Depending on the nature of the organic bromide, the reactions proceeded in acetonitrile (in the case of the aliphatic bromides) or in toluene (in the case of benzyl bromide).

2.2 Biological evaluation

2.2.1 Antimicrobial activity. The antimicrobial (bacteriostatic, fungistatic, bactericidal, and fungicidal) activities of

the synthesized ammonium salts that contain sterically hindered phenolic fragments 4a–e, 5a–e, and 9a and 9b– 16a and 16b were studied *in vitro* in the concentration range of 442–0.70 μM . The results are given in Tables 1 and 2.

The test objects were represented by cultures of Gram-positive bacteria, such as *Staphylococcus aureus* ATCC 209p and *Bacillus cereus* ATCC 8035, Gram-negative bacteria, such as *Escherichia coli* CDC F-50 and *Pseudomonas aeruginosa* ATCC 9027, and fungi, such as *Aspergillus niger* BKM-F-1119, *Trichophyton mentagrophytes* var. *gypseum* 1773, and *Candida albicans* 855-653.

Bacteriostatic and fungistatic activities were investigated using the serial dilution method in liquid nutrient media in accordance with a previously described procedure⁴⁶ by the determination of the minimum inhibitory concentration (MIC) that caused suppression of the growth and reproduction of the test microorganisms. Bactericidal and fungicidal activities, which cause the death of the microbial cells, were determined using literature procedures.^{47,48} The tests were performed in duplicate and repeated twice.

The antibacterial activity of compounds 4a–e, 5a–e, and 9a and 9b– 16a and 16b was observed in the concentration range of 442–0.7 μM . Regarding Gram-positive bacteria, compound 12b was most active; it displayed bactericidal activity with respect to *S. aureus* 209p that exceeded the bactericidal activity of norfloxacin (fluoroquinolone antibiotic) by a factor of 6. Regarding Gram-negative bacteria, the salts 4c, 5c and 12b were most active. According to their bacteriostatic activity, these compounds were superior to chloramphenicol antibiotics by a factor of 14.

The antifungal activity of the objects under study manifested itself in the concentration range of 432–0.9 μM . Compound 5c was found to be the most active; it exhibited fungicidal activity against *C. albicans* at a concentration of 0.9 μM and was thus superior to the reference drug ketoconazole by a factor of 8.

Scheme 2 Synthesis of ammonium salts 4a–e and 5a–e.

Scheme 3 Synthesis of aminophosphonates **7a** and **b** and **8a** and **b**.

Scheme 4 Synthesis of ammonium salts **9a** and **b**–**16a** and **b**.

A large dataset on the antimicrobial activity of the ammonium salts that contain sterically hindered phenolic fragments was obtained, and it was interesting that it revealed some relationships between structural features and activities. It was determined that the substituents on the phosphorus atom and the spacer length did not significantly affect the activities of the salts. An increase in the lipophilic characteristics of the substituent on the quaternary nitrogen atom in the series of ethyl (**4a**, **5a**, **9a**, **9b**, **10a**, **10b**), octyl (**4b**, **5b**), benzyl (**15a**, **15b**, **16a**, **16b**), and decyl resulted in an increase in antimicrobial activity. However, a further increase in the length of the alkyl substituent on the quaternary nitrogen atom from 10 to 12 (**4d**, **5d**, **13a**, **14a**) and 16 (**4e**, **5e**) carbon atoms did not give rise to the expected increase in the activity of the salts. It should be noted that the maximum activity of an ammonium salt among all the types of structure under study was observed in cases in which a decyl group was present on the onium nitrogen atom (**4c**, **5c**, **11a**, **11b**, **12b**). These data are consistent with previous studies of IKhFAN derivatives regarding the effect of the hydrophobicity of the substituent on the quaternary nitrogen atom on their membranotropic properties.²⁶

Thus, we showed that phosphorylated sterically hindered phenols that contain an ammonium fragment displayed higher activity with respect to Gram-positive bacteria (*Staphy-*

lococcus aureus ATCC 209p and *Bacillus cereus* ATCC 8035), whereas analogous phosphorus-free sterically hindered phenols exhibited higher activity with respect to Gram-negative bacteria (*Escherichia coli* CDC F-50 and *Pseudomonas aeruginosa* ATCC 9027) and fungi (*Aspergillus niger* BKMF-1119, *Trichophyton mentagrophytes* var. *gypseum* 1773, and *Candida albicans* 855-653).

2.2.2 Cytotoxicity. An important characteristic in the design of new drugs is their cytotoxic effect with respect to mammalian cells. The cytotoxicity of the ammonium salt derivatives **11a**, **11b**, and **12b**, which exhibited high antimicrobial activity, was determined against WI-38 (human embryonic lung cells) and Chang liver (human liver cells) cell lines. The studies were carried out in the concentration range in which the growth and reproduction of the bacterial and fungal test strains were inhibited. Cytotoxicity was determined by calculating the number of viable WI-38 (human embryonic lung cells) and Chang liver (human liver cells) cells.⁴⁹

As follows from the results in Fig. 2 and 3, only compound **11a** exhibited a cytotoxic effect at its highest concentration (47.0 μ M). At lower concentrations (0.70–11.3 μ M), compounds **11a**, **11b**, and **12b** did not display cytotoxic effects with respect to the WI-38 and Chang liver cell lines.

2.2.3 Antioxidant activity. It is known that antioxidant therapy is indicated in the treatment of a large number of

Table 1 Bacteriostatic and fungistatic activities of ammonium salts **4a–e**, **5a–e**, and **9a** and **9b–16a** and **16b**

Compound	R	n	R'	MIC (μ M)						
				<i>Sa</i>	<i>Bc</i>	<i>Ec</i>	<i>Pa</i>	<i>An</i>	<i>Tm</i>	<i>Ca</i>
4a	—	2	C ₂ H ₅	—	—	—	—	—	—	68.5 $\pm$ 5.8
5a	—	3	C ₂ H ₅	—	—	—	—	—	—	265 $\pm$ 21
4b	—	2	C ₈ H ₁₇	29.0 $\pm$ 2.6	58.0 $\pm$ 5.1	—	—	—	—	29.0 $\pm$ 2.2
5b	—	3	C ₈ H ₁₇	28.0 $\pm$ 2.5	28.1 $\pm$ 2.6	—	—	—	—	28.0 $\pm$ 2.2
4c	—	2	C ₁₀ H ₂₁	1.6 $\pm$ 0.1	6.8 $\pm$ 0.6	27.4 $\pm$ 2.2	27.4 $\pm$ 2.4	—	—	3.3 $\pm$ 0.3
5c	—	3	C ₁₀ H ₂₁	1.5 $\pm$ 0.1	6.7 $\pm$ 0.6	26.8 $\pm$ 2.1	26.8 $\pm$ 2.5	—	—	0.90 $\pm$ 0.08
4d	—	2	C ₁₂ H ₂₅	52.4 $\pm$ 4.0	419 $\pm$ 39	—	—	—	—	419 $\pm$ 37
5d	—	3	C ₁₂ H ₂₅	102 $\pm$ 10	206 $\pm$ 19	—	—	—	—	—
4e	—	2	C ₁₆ H ₃₃	95.7 $\pm$ 8.8	383 $\pm$ 34	—	—	—	—	383 $\pm$ 30
5e	—	3	C ₁₆ H ₃₃	47.0 $\pm$ 4.1	375 $\pm$ 36	—	—	—	—	187 $\pm$ 17
9a	Et	2	C ₂ H ₅	56.8 $\pm$ 4.5	56.8 $\pm$ 5.2	—	—	—	—	—
9b	i-Pr	2	C ₂ H ₅	108 $\pm$ 10	216 $\pm$ 19	—	—	—	—	432 $\pm$ 38
10a	Et	3	C ₂ H ₅	442 $\pm$ 41	221 $\pm$ 21	—	—	—	—	—
10b	i-Pr	3	C ₂ H ₅	105 $\pm$ 9	105 $\pm$ 10	—	—	—	—	422 $\pm$ 33
11a	Et	2	C ₁₀ H ₂₁	2.9 $\pm$ 0.3	2.9 $\pm$ 0.2	94.1 $\pm$ 8.4	94.1 $\pm$ 8.6	—	—	47.0 $\pm$ 4.3
11b	i-Pr	2	C ₁₀ H ₂₁	2.7 $\pm$ 0.3	5.6 $\pm$ 0.4	—	—	—	—	11.3 $\pm$ 0.9
12b	i-Pr	3	C ₁₀ H ₂₁	0.70 $\pm$ 0.06	2.7 $\pm$ 0.2	44.3 $\pm$ 3.9	22 $\pm$ 1.9	—	—	11.0 $\pm$ 0.9
13a	Et	2	C ₁₂ H ₂₅	45.2 $\pm$ 4.2	361 $\pm$ 32	—	—	—	—	45.2 $\pm$ 4.0
14a	Et	3	C ₁₂ H ₂₅	22.0 $\pm$ 1.9	177 $\pm$ 16	—	—	—	—	44.3 $\pm$ 3.9
15a	Et	2	CH ₂ C ₆ H ₅	51.0 $\pm$ 4.7	6.4 $\pm$ 0.6	—	—	—	—	177 $\pm$ 16
15b	i-Pr	2	CH ₂ C ₆ H ₅	24.3 $\pm$ 1.9	48.8 $\pm$ 4.5	—	—	—	—	195 $\pm$ 17
16a	Et	3	CH ₂ C ₆ H ₅	99.5 $\pm$ 9.3	24.8 $\pm$ 2.1	—	—	—	—	199 $\pm$ 19
16b	i-Pr	3	CH ₂ C ₆ H ₅	95.3 $\pm$ 8.5	95.3 $\pm$ 9.1	—	—	—	—	—
Norfloxacin				7.5 $\pm$ 0.6	25.0 $\pm$ 2.2	4.7 $\pm$ 0.3	9.4 $\pm$ 0.9			
Ketoconazole									7.6 $\pm$ 0.5	7.6 $\pm$ 0.6
Chloramphenicol				193 $\pm$ 17	193 $\pm$ 17	386 $\pm$ 35

– high activity that exceeded the activities of pharmaceutical preparations. – high activity that did not exceed the activities of pharmaceutical preparations, although of interest. — did not exhibit biological activity.

diseases. In this case, antioxidants are able to reduce the toxicity and, in some cases, to enhance the activity of drugs.¹⁷ The antiradical properties of the substances were studied using chemiluminescence by a known procedure^{50,51} with a Lum-100 chemiluminometer (OOO DISoft, Russia).

Upon the introduction of solutions of the standard antioxidant ionol into the reaction mixture, the chemiluminescence intensity decreased, which indicates the interaction of the substance with free radicals (Fig. 4). In this case, with an increase in the ionol concentration, there was a decrease in the chemiluminescence intensity. One example was that

at a concentration of 1 mM the chemiluminescence intensity gradually decreased to 24% of the initial value over 10 min (Fig. 4C). Upon the addition of ionol solutions with concentrations of 0.50 and 0.25 mM to the chemiluminescent system, the decrease in the luminescence intensity was drastic, although it only fell to 44% and 64% of the initial value, respectively (Fig. 4B and A). Moreover, there was a slow rise in the chemiluminescence plot upon the introduction of ionol at a concentration of 0.50 mM, which indicates a gradual loss of the ability of the antioxidant to interact with free radicals.

Table 2 Bactericidal and fungicidal activities of ammonium salts **4a–e**, **5a–e**, and **9a** and **9b–16a** and **16b**

Compound	R	n	R'	MIC (μ M)						
				<i>Sa</i>	<i>Bc</i>	<i>Ec</i>	<i>Pa</i>	<i>An</i>	<i>Tm</i>	<i>Ca</i>
4a	—	2	C ₂ H ₅	—	—	—	—	—	—	—
5a	—	3	C ₂ H ₅	—	—	—	—	—	—	265 $\pm$ 21
4b	—	2	C ₈ H ₁₇	29.0 $\pm$ 2.7	58.0 $\pm$ 5.0	—	—	—	—	29.0 $\pm$ 2.4
5b	—	3	C ₈ H ₁₇	28.0 $\pm$ 2.4	28.1 $\pm$ 2.6	—	—	—	—	56.3 $\pm$ 4.9
4c	—	2	C ₁₀ H ₂₁	1.6 $\pm$ 0.1	55.0 $\pm$ 4.3	55.0 $\pm$ 4.8	55.0 $\pm$ 5.1	—	—	6.9 $\pm$ 0.6
5c	—	3	C ₁₀ H ₂₁	3.3 $\pm$ 0.3	107.0 $\pm$ 9.4	53.6 $\pm$ 4.9	26.8 $\pm$ 2.5	—	—	0.90 $\pm$ 0.08
4d	—	2	C ₁₂ H ₂₅	52.4 $\pm$ 4.0	419 $\pm$ 39	—	—	—	—	419 $\pm$ 37
5d	—	3	C ₁₂ H ₂₅	102 $\pm$ 10	206 $\pm$ 19	—	—	—	—	—
4e	—	2	C ₁₆ H ₃₃	—	—	—	—	—	—	383 $\pm$ 30
5e	—	3	C ₁₆ H ₃₃	—	375 $\pm$ 36	—	—	—	—	375 $\pm$ 32
9a	Et	2	C ₂ H ₅	56.8 $\pm$ 4.8	56.8 $\pm$ 4.5	—	—	—	—	—
9b	i-Pr	2	C ₂ H ₅	108 $\pm$ 11	216 $\pm$ 17	—	—	—	—	—
10a	Et	3	C ₂ H ₅	442 $\pm$ 40	221 $\pm$ 22	—	—	—	—	>500
10b	i-Pr	3	C ₂ H ₅	105 $\pm$ 9	421 $\pm$ 37	—	—	—	—	422 $\pm$ 33
11a	Et	2	C ₁₀ H ₂₁	2.9 $\pm$ 0.2	2.9 $\pm$ 0.3	188 $\pm$ 15	—	—	—	47.0 $\pm$ 4.3
11b	i-Pr	2	C ₁₀ H ₂₁	5.6 $\pm$ 0.5	90 $\pm$ 8.4	—	—	—	—	11.3 $\pm$ 0.9
12b	i-Pr	3	C ₁₀ H ₂₁	1.3 $\pm$ 0.1	177 $\pm$ 16	177 $\pm$ 17	44.3 $\pm$ 4.0	—	—	11.0 $\pm$ 0.9
13a	Et	2	C ₁₂ H ₂₅	45.2 $\pm$ 4.4	361 $\pm$ 30	—	—	—	—	45.2 $\pm$ 4.2
14a	Et	3	C ₁₂ H ₂₅	22.0 $\pm$ 2.0	177 $\pm$ 16	—	—	—	—	44.3 $\pm$ 3.9
15a	Et	2	CH ₂ C ₆ H ₅	407 $\pm$ 36	102.0 $\pm$ 9.5	—	—	—	—	177 $\pm$ 16
15b	i-Pr	2	CH ₂ C ₆ H ₅	97.3 $\pm$ 9.0	48.8 $\pm$ 4.3	—	—	—	—	—
16a	Et	3	CH ₂ C ₆ H ₅	199 $\pm$ 18	24.8 $\pm$ 2.1	—	—	—	—	199 $\pm$ 19
16b	i-Pr	3	CH ₂ C ₆ H ₅	95.3 $\pm$ 8.6	95.3 $\pm$ 9.0	—	—	—	—	—
Norfloxacin				7.5 $\pm$ 0.6	50.0 $\pm$ 4.6	4.7 $\pm$ 0.3	48.8 $\pm$ 4.5			
Ketoconazole									15.2 $\pm$ 1.4	15.2 $\pm$ 1.3

– high activity that exceeded the activities of pharmaceutical preparations. – high activity that did not exceed the activities of pharmaceutical preparations, although of interest. — did not exhibit biological activity.

Upon the introduction of compounds **10a**, **11a**, and **12a** into the reaction mixture at a concentration of 0.25 mM, similar patterns were observed in the chemiluminescence curves (Fig. 4A). The maximum decrease in the chemiluminescence intensity in the case of the three tested compounds reached 44% of the initial value, which was more pronounced in comparison with the effect of ionol on the system (the maximum decrease only reached 64% of the initial value). Upon the introduction of **10a**, **11a**, and **12a** into the system at a concentration of 0.50 mM, the following mechanism of the interaction of these compounds with free radicals was observed

(Fig. 4B). The maximum decreases in the chemiluminescence intensity were identical in the case of all three compounds and reached nearly 26% of the initial value, which was more pronounced in comparison with the effect of ionol. In contrast to those for ionol, the chemiluminescence curves that were recorded upon the introduction of the test compounds into the system at concentrations of 0.25 and 0.50 mM continued to fall over the observation period. These results indicate the occurrence of enhanced antioxidant activity in the cases of compounds **10a**, **11a**, and **12a** in comparison with pure ionol. In the case of **12a**, the maximum decrease in the

Fig. 2 Determination of cytotoxic effects of compounds with respect to WI-38 cells. The concentrations of the compounds were as follows (μM): **11a** (2.9; 11.0; 47.0), **11b** (0.70; 2.7; 11.3), and **12b** (0.70; 2.7; 11.0).

chemiluminescence intensity was observed after delays of 400 s at a concentration of 0.25 mM and 500 s at a concentration of 0.50 mM, respectively.

Upon the introduction of the substances into the system at a concentration of 1 mM, the maximum antioxidant activity was observed in the case of compound **11a**, because the maximum decrease in the chemiluminescence intensity to 20% of the initial value was observed under its influence (Fig. 4C) directly after its addition to the system. The antioxidant activities of **10a** and **12a** at a concentration of 1 mM were similar and did not differ from that of ionol at a concentration of 1 mM: the maximum decrease in the chemiluminescence intensity to 26% of the initial value was only observed 600 s after the addition of these compounds to the system (Fig. 4C).

As follows from the results, compounds **10a**, **11a**, and **12a** were able to interact with free radicals and caused a steady decrease in the chemiluminescence intensity of the 2,2'-azobis(2-methylpropionamidine) dihydrochloride (ABAP) + luminol system, which generates free radicals. At low concentrations (0.25 and 0.50 mM), all the substances exhibited enhanced antioxidant activity in comparison with the standard antioxidant ionol. At a concentration of 1 mM, **11a** exhibited

Fig. 3 Determination of cytotoxic effects of compounds with respect to Chang liver cells. The concentrations of the compounds were as follows (μM): **11a** (2.9; 11.0; 47.0), **11b** (0.70; 2.7; 11.3), and **12b** (0.70; 2.7; 11.0).

Fig. 4 Chemiluminescence intensity curves for a system that consisted of ABAP and LM in a buffer solution (total volume of 1.000 mL): the area to the left of the arrow represents the time before the addition of the test substances (baseline); the arrow and the fall of the curve to 0 represent the time of the introduction of the substances; and the increases in the chemiluminescence intensity curves, which are below the baseline, correspond to the interaction of the antioxidant with radicals and their partial inactivation. Plots A, B, and C correspond to chemiluminescence intensity curves for various concentrations of substances: A is 0.25 mM, B is 0.50 mM, and C is 1.00 mM.

the highest activity. Compounds **10a** and **12a** at a concentration of 1 mM acted in a similar way to ionol, with a trend toward a decrease in antioxidant activity. In the case of compound **12a**, lower antioxidant activity was observed.

3. Conclusion

IKhFAN analogues that contain an amide bond have been prepared for the first time *via* the reaction of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-*N*-(2-(dimethylamino)alkyl)-propanamide with aliphatic bromides. It has been shown that the addition of phosphorylated methylenequinones to *N*-nucleophiles (*N,N*-dimethylethane-1,2-diamine and *N,N*-dimethylpropane-1,3-diamine) results in novel organophosphorus compounds that contain a sterically hindered phenolic fragment. The quaternization of α -aminophosphonates that contain a terminal dimethylamino group with monobromides (ethyl, decyl, and dodecyl bromides, as well as benzyl bromide) afforded previously unknown ammonium salts. The antimicrobial activity of a broad range of sterically hindered phenols that contain phosphorylated and ammonium fragments has been studied. It has been determined that phosphorylated sterically hindered phenols that contain an ammonium fragment exhibited higher activity with respect to Gram-positive bacteria (*Staphylococcus aureus* ATCC 209p and *Bacillus cereus* ATCC 8035), whereas similar phosphorus-free sterically hindered phenols exhibited higher activity with respect to Gram-negative bacteria (*Escherichia coli* CDC F-50 and *Pseudomonas aeruginosa* ATCC 9027) and fungi (*Aspergillus niger* BKM-1119, *Trichophyton mentagrophytes* var. *gypseum* 1773, and *Candida albicans* 855-653). The maximum activity of an ammonium salt among all the types of structure was observed in cases in which a decyl radical was present on the onium nitrogen atom (**4c**, **5c**, **11a**, **11b**, **12b**). Compounds **11a**, **11b**, and **12b** did not display cytotoxic properties towards WI-38 and Chang liver cell lines in the concentration range of 0.70–11.3 μ M. Compounds **10a**, **11a**, and **12b** exhibited enhanced antioxidant activity with respect to the standard antioxidant ionol at concentrations of 0.25 and 0.50 mM.

Thus, we have shown that hybrid ammonium salts that contain sterically hindered phenolic and phosphoryl groups are promising classes of compounds for further studies and exhibit high biological activities of various types.

4. Experimental section

4.1 Chemistry

^{13}C NMR spectra were recorded using a Bruker Avance 600 instrument with an operating frequency of 150 MHz. ^1H and ^{31}P NMR spectra were obtained with a Bruker MSL-400 spectrometer operating at a frequency of 400.13 and 161.94 MHz, respectively. Mass spectra (MALDI-TOF) were obtained with a Bruker Ultraflex III TOF/TOF spectrometer (*p*-nitroaniline matrix). IR spectra were recorded using a Bruker Vector 22 Fourier spectrometer in the range of 400–4000

cm^{-1} on KBr pellets. Elemental analysis was performed with a Carlo Erba EA 1108 instrument.

4.1.1 Compounds 2 and 3. Compounds **2** and **3** were synthesized by a literature procedure.⁴⁴

4.1.2 General procedure for the synthesis of compounds 4a–e and 5a–e. To a solution of 0.4 mmol of compound **2** or **3** in 4 mL of acetonitrile, 0.03 mmol of the corresponding bromide was added dropwise. The reaction mixture was maintained at room temperature for 2–3 days; the solvent was removed; and the products were washed with hexane and dried.

4.1.2.1 2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)-*N*-ethyl-*N,N*-dimethylethanaminium bromide (4a). Yield: 0.17 g (93%), mp: 108–110 °C. IR (cm^{-1}): 1654 ($\text{C}=\text{C}_{\text{arom}}$), 3406 (NH), 3641 (OH). ^1H NMR (CDCl_3) δ 1.36 (t, $^3J_{\text{HH}} = 7.4$ Hz, 3H, $\text{N}^+(\text{CH}_2\text{CH}_3)$), 1.42 (s, 18H, $\text{C}(\text{CH}_3)_3$), 2.57 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.85 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.25 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.64 (m, 2H, $\text{N}^+(\text{CH}_2\text{CH}_3)$), 3.72–3.75 (m, 4H, $\text{N}^+(\text{CH}_2\text{CH}_2)$), 5.06 (br.s., 1H, OH), 7.00 (s, 2H, H_{arom}), 8.26 (br.s., NH). ^{13}C NMR (CDCl_3) δ 8.4 ($\text{N}^+(\text{CH}_2\text{CH}_3)$), 30.4 ($\text{C}(\text{CH}_3)_3$), 31.3 ($\text{C}_{\text{arom}}-\text{CH}_2$), 33.7 (NHCH_2), 34.3 ($\text{C}(\text{CH}_3)_3$), 38.2 ($\text{C}(\text{O})\text{CH}_2$), 51.2 ($\text{N}^+(\text{CH}_3)_2$), 60.9 ($\text{N}^+(\text{CH}_2\text{CH}_3)$), 62.1 (NHCH_2CH_2), 124.9 (CH_{arom}), 131.3 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.9 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 152.0 (COH), 173.9 (CO). HRMS (MALDI): calcd for $\text{C}_{23}\text{H}_{41}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$]⁺ 377, found 377. Anal. calcd for $\text{C}_{23}\text{H}_{41}\text{BrN}_2\text{O}_2$ (%): C 60.38; H 9.03; Br 17.47; N 6.12. Found (%): C 60.30; H 9.14; Br 17.41; N 6.04.

4.1.2.2 *N*-(2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)ethyl)-*N,N*-dimethyloctan-1-aminium bromide (4b). Yield: 0.20 g (95%), mp: 32–34 °C. IR (cm^{-1}): 1661 (arom), 3411 (NH), 3644 (OH). ^1H NMR (CDCl_3) δ 0.88 (t, $^3J_{\text{HH}} = 6.5$ Hz, 3H, $\text{N}^+(\text{CH}_2)_7\text{CH}_3$), 1.27–1.34 (m, 10H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3)$), 1.43 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.73 (s, 2H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3)$), 2.58 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.87 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.26 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.48 (m, 2H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3)$), 3.77 (s, 4H, NHCH_2CH_2), 5.05 (br.s., 1H, OH), 7.01 (s, 2H, H_{arom}), 8.30 (br.s., NH). ^{13}C NMR (CDCl_3) δ 14.01 ($\text{N}^+(\text{CH}_2)_7\text{CH}_3$), 22.5, 22.8 ($\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_3)$), 26.2 ($\text{N}^+(\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_3)$), 28.9 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_2(\text{CH}_2)_3$), 30.4 ($\text{C}(\text{CH}_3)_3$), 31.3 ($\text{C}(\text{CH}_3)_3$), 31.3 ($\text{N}^+(\text{CH}_2)_5\text{CH}_2\text{CH}_2\text{CH}_3$), 34.0 (NHCH_2), 34.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 51.6 ($\text{N}^+(\text{CH}_3)_2$), 62.9 (NHCH_2CH_2), 66.0 ($\text{CH}_2\text{N}^+\text{CH}_2$), 124.9 (CH_{arom}), 131.3 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.9 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 152.0 (COH), 174.05 (CO). HRMS (MALDI): calcd for $\text{C}_{29}\text{H}_{53}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$]⁺ 461, found 461. Anal. calcd for $\text{C}_{29}\text{H}_{53}\text{BrN}_2\text{O}_2$ (%): C 64.31; H 9.86; Br 14.75; N 5.17. Found (%): C 65.60; H 10.49; Br 14.81; N 5.00.

4.1.2.3 *N*-(2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)ethyl)-*N,N*-dimethyldodecan-1-aminium bromide (4c). Yield: 0.20 g (88%), mp: 44–46 °C. IR (cm^{-1}): 1663 (arom), 3400 (NH), 3645 (OH). ^1H NMR (CDCl_3) δ 0.89 (t, $^3J_{\text{HH}} = 6.7$ Hz, 3H, $\text{N}^+(\text{CH}_2)_9\text{CH}_3$), 1.26 (br.s., 14H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3)$), 1.43 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.73 (br.s., 2H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3)$), 2.58 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2$), 2.86 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.27 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.49 (m, 2H, $\text{N}^+(\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3)$), 3.76 (s, 4H, NHCH_2CH_2), 5.05 (br.s.,

1H, OH), 7.01 (s, 2H, H_{arom}), 7.79 (br.s., NH). ^{13}C NMR (CDCl_3) δ 14.0 ($\text{N}^+(\text{CH}_2)_9\text{CH}_3$), 22.6 ($\text{N}^+(\text{CH}_2)_8\text{CH}_2\text{CH}_3$), 22.8 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 26.2 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$), 29.1–29.3 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_4$), 30.3 ($\text{C}(\text{CH}_3)_3$), 31.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 31.8 ($\text{N}^+\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_2\text{CH}_3$), 34.0 (NHCH_2), 34.3 ($\text{C}(\text{CH}_3)_3$), 38.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 51.6 ($\text{N}^+(\text{CH}_3)_2$), 62.8 ($\text{CH}_2\text{N}^+\text{CH}_2$), 65.95 ($\text{CH}_2\text{N}^+\text{CH}_2$), 124.9 (CH_{arom}), 131.2 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 152.0 (COH), 174.0 (CO). HRMS (MALDI): calcd for $\text{C}_{31}\text{H}_{57}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 489, found 489. Anal. calcd for $\text{C}_{31}\text{H}_{57}\text{BrN}_2\text{O}_2$ (%): C 65.36; H 10.08; Br 14.03; N 4.92. Found (%): C 65.35; H 10.17; Br 13.96; N 4.85.

4.1.2.4 *N*-(2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)ethyl)-*N,N*-dimethyldodecan-1-aminium bromide (**4d**). Yield: 0.22 g (92%), mp: 38–40 °C. IR (cm^{-1}): 1664 (arom), 3395 (NH), 3647 (OH). ^1H NMR (CDCl_3) δ 0.90 (t, $^3J_{\text{HH}} = 6.7$ Hz, 3H, $\text{N}^+(\text{CH}_2)_{11}\text{CH}_3$), 1.27 (br.s., 18H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 1.44 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.74 (br.s., 2H, $\text{N}^+\text{CH}_2\text{CH}_2$), 2.60 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2$), 2.88 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.25 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.44–3.48 (m, 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_9\text{CH}_3$), 3.79 (s, 4H, $\text{CH}_2\text{N}^+\text{CH}_2$), 5.05 (br.s., 1H, OH), 7.03 (s, 2H, H_{arom}), 8.35 (br.s., 1H, NH). ^{13}C NMR (CDCl_3) δ 14.0 ($\text{N}^+(\text{CH}_2)_{11}\text{CH}_3$), 22.6 ($\text{N}^+(\text{CH}_2)_{10}\text{CH}_2\text{CH}_3$), 22.8 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2$), 26.2 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2$), 29.3, 29.6 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_7$), 30.3 ($\text{C}(\text{CH}_3)_3$), 31.9 ($\text{N}^+(\text{CH}_2)_{10}\text{CH}_2$), 34.0 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 34.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.3 (NHCH_2CH_2), 51.6 ($\text{N}^+(\text{CH}_3)_2$), 62.9 (NHCH_2CH_2), 66.2 ($\text{CH}_2\text{N}^+\text{CH}_2$), 125.0 (CH_{arom}), 131.2 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 152.0 (COH), 174.0 (CO). HRMS (MALDI): calcd for $\text{C}_{33}\text{H}_{61}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 517, found 517. Anal. calcd for $\text{C}_{33}\text{H}_{61}\text{BrN}_2\text{O}_2$ (%): C 66.31; H 10.29; Br 13.37; N 4.69. Found (%): C 66.33; H 10.21; Br 13.42; N 4.54.

4.1.2.5 *N*-(2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)ethyl)-*N,N*-dimethylhexadecan-1-aminium bromide (**4e**). Yield: 0.24 g (92%), mp: 32–34 °C. IR (cm^{-1}): 1652 (arom), 3410 (NH), 3645 (OH). ^1H NMR (CDCl_3) δ 0.88 (t, $^3J_{\text{HH}} = 7.13$ Hz, 3H, $\text{N}^+(\text{CH}_2)_{15}\text{CH}_3$), 1.26–1.30 (m, 26H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 1.42 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.72 (br.s., 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 2.58 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.86 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.26 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.48 (m, 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 3.77 (s, 4H, $\text{NHCH}_2\text{CH}_2\text{N}^+$), 5.05 (br.s., 1H, OH), 7.01 (s, 2H, H_{arom}), 8.29 (br.s., 1H, NH). ^{13}C NMR (CDCl_3) δ 14.1 ($\text{N}^+(\text{CH}_2)_{15}\text{CH}_3$), 22.7 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_{13}\text{CH}_3$), 22.7 ($\text{N}^+(\text{CH}_2)_{14}\text{CH}_2\text{CH}_3$), 26.3 ($\text{N}^+(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_{12}\text{CH}_3$), 29.4 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_9(\text{CH}_2)_2\text{CH}_3$), 30.4 ($\text{C}(\text{CH}_3)_3$), 31.4 ($\text{C}(\text{CH}_3)_3$), $\text{N}^+(\text{CH}_2)_{13}\text{CH}_2\text{CH}_2\text{CH}_3$), 31.9 (NHCH_2CH_2), 34.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.4 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 51.6 ($\text{N}^+(\text{CH}_3)_2$), 62.7 (NHCH_2CH_2), 66.0 ($\text{CH}_2\text{N}^+\text{CH}_2$), 125.0 (CH_{arom}), 131.3 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 152.0 (COH), 174.0 (CO). HRMS (MALDI): calcd for $\text{C}_{37}\text{H}_{69}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 573, found 573. Anal. calcd for $\text{C}_{37}\text{H}_{69}\text{BrN}_2\text{O}_2$ (%): C 67.96; H 10.64; Br 12.22; N 4.28. Found (%): C 68.03; H 10.71; Br 12.16; N 4.34.

4.1.2.6 3-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)-*N*-ethyl-*N,N*-dimethylpropan-1-aminium bromide (**5a**). Yield: 0.17 g (90%), mp: 46–48 °C. IR (cm^{-1}): 1652 ($\text{C}=\text{C}_{\text{arom}}$), 1725 (CO), 3425 (NH), 3641 (OH). ^1H NMR (CDCl_3) δ 1.39–1.40 (m, 21H, $\text{N}^+\text{CH}_2\text{CH}_3$, $\text{C}(\text{CH}_3)_3$), 2.06–2.09

(m, 2H, $\text{NHCH}_2\text{CH}_2\text{CH}_2$), 2.61 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.88 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.23 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.39 (m, 2H, $\text{N}^+\text{CH}_2\text{CH}_3$), 3.52–3.56 (m, 2H, $\text{NH}(\text{CH}_2)_2\text{CH}_2$), 3.81 (m, 2H, $\text{NHCH}_2(\text{CH}_2)_2$), 5.05 (br.s., 1H, OH), 7.03 (s, 2H, H_{arom}), 8.26 (br.s., NH). ^{13}C NMR (CDCl_3) δ 8.5 ($\text{N}^+\text{CH}_2\text{CH}_3$), 22.8 (NHCH_2CH_2), 30.4 ($\text{C}(\text{CH}_3)_3$), 31.7 ($\text{C}_{\text{arom}}-\text{CH}_2$), 34.3 ($\text{C}(\text{CH}_3)_3$), 36.1 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.5 (NHCH_2), 50.4 ($\text{N}^+(\text{CH}_3)_2$), 60.1 ($\text{N}^+\text{CH}_2\text{CH}_3$), 62.3 ($\text{CH}_2\text{N}^+\text{CH}_2$), 125.0 (CH_{arom}), 131.6 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 151.9 (COH), 173.9 (CO). HRMS (MALDI): calcd for $\text{C}_{24}\text{H}_{43}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 391, found 391. Anal. calcd for $\text{C}_{24}\text{H}_{43}\text{BrN}_2\text{O}_2$ (%): C 61.13; H 9.69; Br 16.95; N 6.42. Found (%): C 61.09; H 9.72; Br 16.87; N 6.53.

4.1.2.7 *N*-(3-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)propyl)-*N,N*-dimethyloctan-1-aminium bromide (**5b**). Yield: 0.20 g (90%), mp: 30–32 °C. IR (cm^{-1}): 1660 (arom), 1725 (CO), 3645 (OH). ^1H NMR (CDCl_3) δ 0.87 (t, $^3J_{\text{HH}} = 5.59$ Hz, 3H, $\text{N}^+(\text{CH}_2)_7\text{CH}_3$), 1.26–1.35 (m, 10H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 1.42 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.72 (br.s., 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_3$), 2.08 (br.s., 2H, $\text{NHCH}_2\text{CH}_2\text{CH}_2$), 2.59 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.86 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 3.26 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.37–3.39 (m, 4H, $\text{CH}_2\text{N}^+\text{CH}_2$), 3.80 (m, 2H, NHCH_2), 5.03 (br.s., 1H, OH), 7.02 (s, 2H, H_{arom}), 7.80 (br.s., NH). ^{13}C NMR (CDCl_3) δ 14.00 ($\text{N}^+(\text{CH}_2)_7\text{CH}_3$), 22.5, 22.8 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_3$), 26.3 ($\text{NHCH}_2\text{CH}_2\text{CH}_2$), 28.9–29.0 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{CH}_3$), 30.4 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_2(\text{CH}_2)_3$), 31.6 ($\text{C}(\text{CH}_3)_3$), 31.7 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 36.1 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.6 (NHCH_2), 51.0 ($\text{N}^+(\text{CH}_3)_2$), 63.0 ($\text{NHCH}_2\text{CH}_2\text{CH}_2$), 64.9 ($\text{CH}_2\text{N}^+\text{CH}_2$), 125.0 (CH_{arom}), 131.6 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 151.9 (COH), 174.0 (CO). HRMS (MALDI): calcd for $\text{C}_{30}\text{H}_{55}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 475, found 475. Anal. calcd for $\text{C}_{30}\text{H}_{55}\text{BrN}_2\text{O}_2$ (%): C 64.84; H 9.98; Br 14.38; N 5.04. Found (%): C 64.80; H 10.03; Br 14.44; N 4.98.

4.1.2.8 *N*-(3-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)propyl)-*N,N*-dimethyldecan-1-aminium bromide (**5c**). Yield: 0.21 g (90%), mp: 116–118 °C. IR (cm^{-1}): 1660 (arom), 3400 (NH), 3647 (OH). ^1H NMR (CDCl_3) δ 0.89 (t, $^3J_{\text{HH}} = 6.9$ Hz, 3H, $\text{N}^+(\text{CH}_2)_9\text{CH}_3$), 1.27–1.36 (m, 14H, $\text{N}^+(\text{CH}_2)_7\text{CH}_3$), 1.43 (s, 18H, $\text{C}(\text{CH}_3)_3$), 1.73 (br.s., 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$), 2.09 (br.s., 2H, NHCH_2CH_2), 2.60–2.63 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 2.86–2.89 (m, 2H, $\text{C}_{\text{arom}}-\text{CH}_2$), 3.25 (s, 6H, $\text{N}^+(\text{CH}_3)_2$), 3.24–3.42 (m, 4H, $\text{CH}_2\text{N}^+\text{CH}_2$), 3.80–3.84 (m, 2H, NHCH_2), 5.04 (br.s., 1H, OH), 7.03 (s, 2H, H_{arom}), 7.79 (br.s., NH). ^{13}C NMR (CDCl_3) δ 14.0 ($\text{N}^+\text{CH}_2\text{CH}_3$), 22.7, 22.6 ($\text{CH}_2\text{CH}_2\text{N}^+\text{CH}_2\text{CH}_3$), 26.2 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2$), 29.1 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2$), 29.3 ($\text{N}^+(\text{CH}_2)_3(\text{CH}_2)_4$), 30.1 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_3$), 30.9 ($\text{C}_{\text{arom}}-\text{CH}_2$), 31.3 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 36.1 ($\text{C}_{\text{arom}}-\text{CH}_2\text{CH}_2$), 38.5 (NHCH_2), 50.9 ($\text{N}^+(\text{CH}_3)_2$), 62.9 ($\text{CH}_2\text{N}^+\text{CH}_2$), 64.8 ($\text{CH}_2\text{N}^+\text{CH}_2$), 124.9 (CH_{arom}), 131.6 ($\text{C}_{\text{arom}}-\text{CH}_2$), 135.8 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 151.9 (COH), 173.92 (CO). HRMS (MALDI): calcd for $\text{C}_{32}\text{H}_{59}\text{N}_2\text{O}_2$ [$\text{M} - \text{Br}$] $^+$ 503, found 503. Anal. calcd for $\text{C}_{32}\text{H}_{59}\text{BrN}_2\text{O}_2$ (%): C 65.84; H 10.19; Br 13.69; N 4.80. Found (%): C 65.75; H 10.21; Br 13.61; N 4.75.

4.1.2.9 *N*-(3-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)propyl)-*N,N*-dimethyldodecan-1-aminium bromide (**5d**). Yield: 0.23 g (94%), mp: 44–46 °C. IR (cm^{-1}): 1658 (arom), 3404 (NH), 3647 (OH). ^1H NMR (CDCl_3) δ 0.90 (t, $^3J_{\text{HH}}$

= 6.7 Hz, 3H, $N^+(CH_2)_{11}CH_3$), 1.28 (br.s., 18H, $N^+CH_2CH_2(CH_2)_9CH_3$), 1.44 (s, 18H, $C(CH_3)_3$), 1.75 (br.s., 2H, $N^+CH_2CH_2(CH_2)_9CH_3$), 2.09 (br.s., 2H, $NHCH_2CH_2CH_2N^+$), 2.61 (m, 2H, $C_{arom}-CH_2CH_2$), 2.87 (m, 2H, $C_{arom}-CH_2$), 3.24 (s, 6H, $N^+(CH_3)_2$), 3.33–3.40 (m, 4H, $CH_2N^+CH_2$), 3.84 (m, 2H, $NHCH_2$), 5.04 (br.s., 1H, OH), 7.06 (s, 2H, H_{arom}). ^{13}C NMR ($CDCl_3$) δ 14.0 ($N^+(CH_2)_{11}CH_3$), 22.8, 22.7 ($CH_2CH_2N^+(CH_2)_{10}CH_2CH_3$), 26.1 ($N^+CH_2CH_2CH_2$), 26.2 ($N^+CH_2CH_2CH_2$), 29.6, 29.3 ($N^+(CH_2)_3(CH_2)_6$), 30.4 ($C(CH_3)_3$), 31.7 ($C_{arom}-CH_2CH_2$), 31.9 ($N^+(CH_2)_9CH_2$), 34.3 ($C(CH_3)_3$), 36.1 ($C_{arom}-CH_2CH_2$), 38.6 ($NHCH_2$), 50.9 ($N^+(CH_3)_2$), 62.9 ($CH_2N^+CH_2$), 64.8 ($CH_2N^+CH_2$), 125.0 (C_{arom}), 131.6 ($C_{arom}-CH_2$), 135.7 ($C_{arom}-C(CH_3)_3$), 151.9 (COH), 173.9 (CO). HRMS (MALDI): calcd for $C_{33}H_{61}BrN_2O_2$ [$M - Br$] $^+$ 531, found 531. Anal. calcd for $C_{33}H_{61}BrN_2O_2$ (%): C 66.75; H 10.38; Br 13.06; N 4.58. Found (%): C 66.77; H 10.31; Br 12.99; N 4.45.

4.1.2.10 *N*-(2-(3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-propanamido)ethyl)-*N,N*-dimethylhexadecan-1-aminium bromide (5e). Yield: 0.24 g (90%), mp: 28–30 °C. IR (cm^{-1}): 1653 (arom), 3408 (NH), 3646 (OH). 1H NMR ($CDCl_3$) δ 0.88 (t, $^3J_{HH} = 6.3$ Hz, 3H, $N^+(CH_2)_{15}CH_3$), 1.25 (br.s., 26H, $N^+CH_2CH_2(CH_2)_{13}CH_3$), 1.42 (s, 18H, $C(CH_3)_3$), 1.72 (br.s., 2H, $N^+CH_2CH_2(CH_2)_{13}CH_3$), 2.07 (br.s., 2H, $NHCH_2CH_2CH_2N^+$), 2.60 (m, 2H, $C_{arom}-CH_2CH_2$), 2.87 (m, 2H, $C_{arom}-CH_2CH_2$), 3.24 (s, 6H, $N^+(CH_3)_2$), 3.32–3.39 (m, 4H, $CH_2N^+CH_2$), 3.82 (m, 2H, $NHCH_2$), 5.03 (br.s., 1H, OH), 7.02 (s, 2H, H_{arom}), 8.29 (br.s., 1H, NH). ^{13}C NMR ($CDCl_3$) δ 14.1 ($N^+(CH_2)_{15}CH_3$), 22.6 ($N^+CH_2CH_2(CH_2)_{13}CH_2CH_3$), 22.8 ($NHCH_2CH_2CH_2$), 26.3 ($N^+(CH_2)_2CH_2(CH_2)_{12}CH_3$), 29.1 ($N^+(CH_2)_3(CH_2)_9(CH_2)_2CH_3$), 29.3 ($N^+(CH_2)_{13}CH_2CH_2CH_3$), 30.4 ($C(CH_3)_3$), 31.9 ($C(CH_3)_3$), 34.3 ($C_{arom}-CH_2CH_2$), 36.2 ($C_{arom}-CH_2CH_2$), 38.6 ($NHCH_2CH_2$), 51.0 ($N^+(CH_3)_2$), 62.9 ($NH(CH_2)_2CH_2$), 64.8 ($CH_2N^+CH_2$), 125.0 (C_{arom}), 131.7 ($C_{arom}-CH_2$), 135.8 ($C_{arom}-C(CH_3)_3$), 151.9 (COH), 173.9 (CO). HRMS (MALDI): calcd for $C_{33}H_{61}N_2O_2$ [$M - Br$] $^+$ 587, found 587. Anal. calcd for $C_{33}H_{61}BrN_2O_2$ (%): C, 68.34; H, 10.71; Br, 11.96; N, 4.19. Found (%): C, 68.28; H, 10.75; Br, 11.90; N, 4.23.

4.1.3 General procedure for the synthesis of compounds 7a and b and 8a and b. To a solution of 1.12 mmol of the appropriate methylenequinone 6a or b in 3 mL of methylene dichloride, 1.09 mmol of the corresponding amine (*N,N*-dimethyl-1,2-diaminoethane or *N,N*-dimethyl-1,3-diaminopropane) was added dropwise. The reaction mixture was maintained at room temperature for 5 h in a dry argon flow; the solvent was removed; and the products were washed with pentane and dried.

4.1.3.1 Diethyl ((3,5-di-*tert*-butyl-4-hydroxyphenyl)((2-(dimethylamino)ethyl)amino)methyl)phosphonate (7a). Yield: 0.50 g (100%), mp: 83–85 °C. IR (cm^{-1}): 1056 (POC), 1236 (PO), 1654 (arom), 3367 (NH), 3612 (OH). 1H NMR ($CDCl_3$) δ 1.09 (t, $^3J_{HH} = 7.1$ Hz, 3H, CH_3), 1.25 (t, $^3J_{HH} = 7.1$ Hz, 3H, CH_3), 1.41 (s, 18H, *t*-Bu), 2.14 (s, 6H, $N(CH_3)_2$), 2.23 (s, 1H, NH), 2.36 (m, 2H, NCH_2), 2.57 (m, 2H, $NHCH_2$), 3.91 (d, $^2J_{PH} = 19.0$ Hz, 1H, CH), 3.76–4.05 (m, 4H, OCH_2), 5.15 (br.s., 1H, OH), 7.16 (d, $^4J_{PH} = 2.3$ Hz, 2H, H_{arom}). ^{13}C NMR ($CDCl_3$) δ 16.1 (CH_3), 16.2 (CH_3), 16.3 (CH_3), 16.4 (CH_3), 30.3 ($C(CH_3)_3$),

34.3 ($C(CH_3)_3$), 45.3 ($N(CH_3)_2$), 45.4 ($NHCH_2$), 45.6 ($NHCH_2$), 58.9 (NCH_2), 61.2 (CH, $J_{PC} = 154.1$ Hz), 62.3 (OCH_2 , $J_{PC} = 6.6$ Hz), 62.4 (OCH_2 , $J_{PC} = 6.9$ Hz), 125.0 ($C_{arom}CH$, $J_{PC} = 6.3$ Hz), 126.3 (CH_{arom} , $J_{PC} = 3.5$ Hz), 135.8 ($C_{arom}C(CH_3)_3$, $J_{PC} = 1.6$ Hz), 154.3 ($C_{arom}OH$, $J_{PC} = 3.2$ Hz). ^{31}P NMR ($CDCl_3$) δ 24.9. HRMS (MALDI): calcd for $C_{23}H_{43}N_2O_4P$ [M] $^+$ 443, found 443. Anal. calcd for $C_{23}H_{43}N_2O_4P$ (%): C, 62.42; H, 9.79; N, 6.33; P, 7.00. Found (%): C, 62.48; H, 9.83; N, 6.30; P, 6.95.

4.1.3.2 Diisopropyl ((3,5-di-*tert*-butyl-4-hydroxyphenyl)((2-(dimethylamino)ethyl)amino)methyl)phosphonate (7b). Yield: 0.52 g (99%), mp: 82–84 °C. IR (cm^{-1}): 1049 (POC), 1234 (PO), 1650 (arom), 3362 (NH), 3610 (OH). 1H NMR ($CDCl_3$) δ 0.94 (d, $^3J_{HH} = 6.2$ Hz, 3H, $OCH(CH_3)_2$), 1.22 (d, $^3J_{HH} = 6.2$ Hz, 3H, $OCH(CH_3)_2$), 1.26 (d, $^3J_{HH} = 6.2$ Hz, 3H, $OCH(CH_3)_2$), 1.27 (d, $^3J_{HH} = 6.2$ Hz, 3H, $OCH(CH_3)_2$), 1.42 (s, 18H, *t*-Bu), 2.20 (s, 6H, $N(CH_3)_2$), 2.4 (m, 2H, $NHCH_2CH_2$), 2.6 (m, 2H, $NHCH_2$), 3.85 (d, $^2J_{PH} = 19.0$ Hz, 1H, CH), 4.46 (m, 1H, OCH), 4.66 (m, 1H, OCH), 5.13 (s, 1H, OH), 7.18 (d, $^4J_{PH} = 2.1$ Hz, 2H, H_{arom}). ^{13}C NMR ($CDCl_3$) δ 23.3 (CH_3), 23.9 (CH_3), 24.1 (CH_3), 24.3 (CH_3), 30.3 ($C(CH_3)_3$), 34.3 ($C(CH_3)_3$), 45.3 ($N(CH_3)_2$), 45.6 ($NHCH_2$), 45.7 ($NHCH_2$), 58.9 (NCH_2), 61.7 (CH, $J_{PC} = 155.7$ Hz), 70.8 (OCH_2 , $J_{PC} = 7.4$ Hz), 71.0 (OCH_2 , $J_{PC} = 7.1$ Hz), 125.3 ($C_{arom}CH$, $J_{PC} = 6.4$ Hz), 126.7 (CH_{arom} , $J_{PC} = 2.7$ Hz), 135.6 ($C_{arom}C(CH_3)_3$, $J_{PC} = 1.8$ Hz), 154.3 ($C_{arom}OH$, $J_{PC} = 3.0$ Hz). ^{31}P NMR ($CDCl_3$) δ 22.9. HRMS (MALDI): calcd for $C_{25}H_{47}N_2O_4P$ [M] $^+$ 471, found 471. Anal. calcd for $C_{25}H_{47}N_2O_4P$ (%): C, 63.80; H, 10.07; N, 5.95; P, 6.58. Found (%): C, 63.72; H, 9.99; N, 6.09; P, 6.63.

4.1.3.3 Diethyl ((3,5-di-*tert*-butyl-4-hydroxyphenyl)((3-(dimethylamino)propyl)amino)methyl)phosphonate (8a). Yield: 0.49 g (97%), mp: 100–101 °C. IR (cm^{-1}): 1050 (POC), 1235 (PO), 1656 (arom), 3360 (NH), 3616 (OH). 1H NMR ($CDCl_3$) δ 1.21 (t, $^3J_{HH} = 7.06$ Hz, 3H, CH_3), 1.27 (t, $^3J_{HH} = 7.06$ Hz, 3H, CH_3), 1.43 (s, 18H, *t*-Bu), 1.64 (m, $NHCH_2CH_2CH_2$), 2.21 (s, 6H, $N(CH_3)_2$), 2.24–2.36 (m, 2H, CH_2N), 2.58 (m, 2H, $NHCH_2$), 3.79 (m, 1H, CH), 3.95 (m, 2H, OCH_2), 4.03 (m, 2H, OCH_2), 5.16 (s, 1H, OH), 7.17 (d, $^4J_{PH} = 2.08$ Hz, 2H, H_{arom}). ^{13}C NMR ($CDCl_3$) δ 16.2 (CH_3), 16.3 (CH_3), 16.4 (CH_3), 16.5 (CH_3), 27.8 ($NHCH_2CH_2CH_2$), 30.3 ($C(CH_3)_3$), 34.3 ($C(CH_3)_3$), 45.2 ($NHCH_2$), 45.3 ($N(CH_3)_2$), 45.5 ($NHCH_2$), 58.8 (NCH_2), 61.0 (CH, $J_{PC} = 153.3$ Hz), 62.5 (OCH_2 , $J_{PC} = 6.6$ Hz), 62.6 (OCH_2 , $J_{PC} = 6.9$ Hz), 124.0 ($C_{arom}CH$, $J_{PC} = 6.1$ Hz), 126.1 (CH_{arom} , $J_{PC} = 4.2$ Hz), 135.7 ($C_{arom}-C(CH_3)_3$, $J_{PC} = 2.4$ Hz), 154.3 ($C_{arom}OH$, $J_{PC} = 3.4$ Hz). ^{31}P NMR ($CDCl_3$) δ 24.3. HRMS (MALDI): calcd for $C_{24}H_{45}N_2O_4P$ [M] $^+$ 456, found 456. Anal. calcd for $C_{24}H_{45}N_2O_4P$ (%): C, 63.13; H, 9.93; N, 6.14; P, 6.78. Found (%): C, 63.22; H, 9.89; N, 6.33; P, 7.00.

4.1.3.4 Diisopropyl ((3,5-di-*tert*-butyl-4-hydroxyphenyl)((3-(dimethylamino)propyl)amino)methyl)phosphonate (8b). Yield: 0.52 g (97%), mp: 84–86 °C. IR (cm^{-1}): 1055 (POC), 1230 (PO), 1657 (arom), 3366 (NH), 3610 (OH). 1H NMR ($CDCl_3$) δ 0.94 (d, $^3J_{HH} = 6.18$ Hz, 3H, $OCH(CH_3)_2$), 1.21 (d, $^3J_{HH} = 6.18$ Hz, 3H, $OCH(CH_3)_2$), 1.25 (d, $^3J_{HH} = 6.18$ Hz, 3H, $OCH(CH_3)_2$), 1.26 (d, $^3J_{HH} = 6.18$ Hz, 3H, $OCH(CH_3)_2$), 1.42 (s, 18H, *t*-Bu), 1.63 (m, 2H, $NHCH_2CH_2CH_2$), 2.20 (s, 6H, $N(CH_3)_2$), 2.28 (m, 2H, NCH_2), 2.56 (m, 2H, $NHCH_2$), 3.84 (d, $^2J_{PH} = 19.0$ Hz, 1H,

CH), 4.45 (m, 1H, OCH), 4.65 (m, 1H, OCH), 5.13 (s, 1H, OH), 7.12 (d, $^4J_{\text{PH}} = 1.9$ Hz, 2H, H_{arom}). ^{13}C NMR (CDCl_3) δ 23.3 (CH_3), 23.9 (CH_3), 24.1 (CH_3), 24.3 (CH_3), 27.9 ($\text{NHCH}_2\text{CH}_2\text{CH}_2$), 30.3 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 45.4 ($\text{N}(\text{CH}_3)_2$), 46.3 (NHCH_2), 46.4 (NHCH_2), 57.9 (NCH_2), 61.5 (CH , $J_{\text{PC}} = 155.2$ Hz), 70.8 (OCH_2 , $J_{\text{PC}} = 7.3$ Hz), 71.0 (OCH_2 , $J_{\text{PC}} = 7.1$ Hz), 125.2 (C_{aromCH} , $J_{\text{PC}} = 6.3$ Hz), 126.7 (CH_{arom} , $J_{\text{PC}} = 3.5$ Hz), 135.6 ($\text{C}_{\text{aromC}}(\text{CH}_3)_3$, $J_{\text{PC}} = 1.8$ Hz), 153.3 (C_{aromOH} , $J_{\text{PC}} = 3.1$ Hz). ^{31}P NMR (CDCl_3) δ 22.9. HRMS (MALDI): calcd for $\text{C}_{26}\text{H}_{49}\text{N}_2\text{O}_4\text{P}$ $[\text{M}]^+$ 483, found 483. Anal. calcd for $\text{C}_{26}\text{H}_{49}\text{N}_2\text{O}_4\text{P}$ (%): C, 64.43; H, 10.19; N, 5.78; P, 6.39. Found (%): C, 64.42; H, 10.25; N, 5.69; P, 6.34.

4.1.4 General procedure for the synthesis of compounds 9a and 9b–16a and 16b. To a solution of 0.23 mmol of compound 7a or b or 8a or b in 2 mL of acetonitrile/toluene, 0.3 mmol of the corresponding alkyl bromide was added dropwise. The reaction mixture was maintained at room temperature for 12 h in a dry argon flow. The solvent was removed, and the light-yellow product was washed with diethyl ether and dried.

4.1.4.1 2-(((3,5-Di-tert-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)-N-ethyl-N,N-dimethylethan-1-aminium bromide (9a). Yield: 0.12 g (95%), mp: 92–93 °C. IR (cm^{-1}): 1024 (POC), 1237 (PO), 1653 (arom), 3634 (OH). ^1H NMR (CD_3OD) δ 1.13 (t, $^3J_{\text{HH}} = 6.6$ Hz, 3H, OCH_2CH_3), 1.31 (t, $^3J_{\text{HH}} = 6.8$ Hz, 3H, OCH_2CH_3), 1.36 (t, $^3J_{\text{HH}} = 7.0$ Hz, 3H, $\text{N}^+\text{CH}_2\text{CH}_3$), 1.46 (s, 18H, *t*-Bu), 2.98–3.07 (m, 2H, NHCH_2), 3.16 (s, 6H, N^+CH_3), 3.44–3.50 (m, 4H, N^+CH_2 , $\text{N}^+\text{CH}_2\text{CH}_3$), 3.81–4.11 (m, 5H, OCH_2 , CH), 7.27 (d, $^4J_{\text{PH}} = 2.1$ Hz, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 7.3 ($\text{N}^+\text{CH}_2\text{CH}_3$), 7.4 ($\text{N}^+\text{CH}_2\text{CH}_3$), 15.4 (CH_3), 15.6 (CH_3), 29.6 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 41.4 (NHCH_2), 41.5 (NHCH_2), 50.4 ($\text{N}^+(\text{CH}_3)_2$), 59.6 (CH, $J_{\text{PC}} = 157.2$ Hz), 60.4 ($\text{N}^+\text{CH}_2\text{CH}_3$), 61.9 (NCH_2), 62.6 (OCH_2 , $J_{\text{PC}} = 7.5$ Hz), 63.0 (OCH_2 , $J_{\text{PC}} = 7.2$ Hz), 125.1 (C_{aromCH} , $J_{\text{PC}} = 6.4$ Hz), 125.4 (CH_{arom} , $J_{\text{PC}} = 2.3$ Hz), 138.2 ($\text{C}_{\text{aromC}}(\text{CH}_3)_3$, $J_{\text{PC}} = 2.0$ Hz), 154.1 (C_{aromOH} , $J_{\text{PC}} = 3.1$ Hz). ^{31}P NMR (CD_3OD) δ 24.2. HRMS (MALDI): calcd for $\text{C}_{25}\text{H}_{48}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 471, found 471. Anal. calcd for $\text{C}_{25}\text{H}_{48}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 54.44; H, 8.77; Br, 14.49; N, 5.08; P, 5.62. Found (%): C, 54.48; H, 8.83; Br, 14.57; N, 5.01; P, 5.53.

4.1.4.2 2-(((3,5-Di-tert-butyl-4-hydroxyphenyl)-(diisopropoxyphosphoryl)methyl)amino)-N-ethyl-N,N-dimethylethan-1-aminium bromide (9b). Yield: 0.13 g (96%), mp: 109–111 °C. IR (cm^{-1}): 1026 (POC), 1234 (PO), 1655 (arom), 3621 (OH). ^1H NMR (CD_3OD) δ 0.94 (d, $^3J_{\text{HH}} = 6.2$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.25 (d, $^3J_{\text{HH}} = 6.2$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.30–1.33 (m, 6H, $\text{N}^+\text{CH}_2\text{CH}_3$, $\text{OCH}(\text{CH}_3)_2$), 1.46 (s, 18H, *t*-Bu), 2.97–3.06 (m, 2H, NHCH_2), 3.14 (s, 6H, N^+CH_3), 3.40–3.49 (m, 4H, N^+CH_2 , $\text{N}^+\text{CH}_2\text{CH}_3$), 3.99 (d, $^2J_{\text{PH}} = 20.2$ Hz, 1H, CH), 4.40 (m, 1H, OCH), 4.67 (m, 1H, OCH), 7.26 (d, $^4J_{\text{PH}} = 2.0$ Hz, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 7.4 ($\text{N}^+\text{CH}_2\text{CH}_3$), 22.5 (CH_3), 23.1 (CH_3), 23.2 (CH_3), 23.3 (CH_3), 29.5 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 41.5 (NHCH_2), 41.6 (NHCH_2), 50.4 ($\text{N}^+(\text{CH}_3)_2$), 60.4 (CH, $J_{\text{PC}} = 159.0$ Hz), 60.4 ($\text{N}^+\text{CH}_2\text{CH}_3$), 61.9 (NCH_2), 71.2 (OCH), 72.0 (OCH), 125.4 (C_{aromCH}), 125.7 (CH_{arom}), 138.1 ($\text{C}_{\text{aromC}}(\text{CH}_3)_3$), 154.1 (C_{aromOH}). ^{31}P NMR (CD_3OD) δ 21.6. HRMS (MALDI): calcd for $\text{C}_{27}\text{H}_{52}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 499, found 499. Anal. calcd for

$\text{C}_{27}\text{H}_{52}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 55.95; H, 9.04; Br, 13.79; N, 4.83; P, 5.34. Found (%): C, 55.91; H, 9.10; Br, 13.72; N, 4.86; P, 5.31.

4.1.4.3 3-(((3,5-Di-tert-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)-N-ethyl-N,N-dimethylpropan-1-aminium bromide (10a). Yield: 0.12 g (92%), mp: 95–98 °C. IR (cm^{-1}): 1029 (POC), 1216 (PO), 1624 (arom), 3423 (NH). ^1H NMR (CD_3OD) δ 1.12 (t, $^3J_{\text{HH}} = 7.04$ Hz, 3H, OCH_2CH_3), 1.31 (t, $^3J_{\text{HH}} = 7.05$ Hz, 3H, OCH_2CH_3), 1.36 (t, $^3J_{\text{HH}} = 7.07$ Hz, 3H, $\text{N}^+\text{CH}_2\text{CH}_3$), 1.45 (s, 18H, *t*-Bu), 1.94 (m, 2H, $\text{NHCH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.68 (m, 2H, NHCH_2), 3.09 (s, 6H, NCH_3), 3.44 (m, 4H, N^+CH_2 , $\text{N}^+\text{CH}_2\text{CH}_3$), 3.80–4.11 (m, 4H, OCH_2), 4.04 (d, $^2J_{\text{PH}} = 19.49$ Hz, 1H, CH), 7.26 (d, $^4J_{\text{PH}} = 1.91$ Hz, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 7.2 ($\text{N}^+\text{CH}_2\text{CH}_3$), 15.3 (CH_3), 15.4 (CH_3), 15.5 (CH_3), 15.6 (CH_3), 22.4 ($\text{NHCH}_2\text{CH}_2\text{CH}_2\text{N}$), 29.5 ($\text{C}(\text{CH}_3)_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 41.1 (NHCH_2), 41.3 (NHCH_2), 49.6 ($\text{N}^+(\text{CH}_3)_2$), 59.5 ($\text{N}^+\text{CH}_2\text{CH}_3$), 60.0 (CH, $J_{\text{PC}} = 155.2$ Hz), 61.9 (NCH_2), 62.7 (OCH_2 , $J_{\text{PC}} = 7.5$ Hz), 63.0 (OCH_2 , $J_{\text{PC}} = 7.3$ Hz), 125.0 (C_{aromCH}), 125.8 (CH_{arom}), 138.1 ($\text{C}_{\text{aromC}}(\text{CH}_3)_3$), 153.9 (C_{aromOH}). ^{31}P NMR (CD_3OD) δ 24.6. HRMS (MALDI): calcd for $\text{C}_{26}\text{H}_{50}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 485, found 485. Anal. calcd for $\text{C}_{26}\text{H}_{50}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 55.22; H, 8.91; N, 4.95; P, 5.48; Br, 14.13. Found (%): C, 55.17; H, 9.02; N, 5.14; P, 5.68; Br, 14.08.

4.1.4.4 3-(((3,5-Di-tert-butyl-4-hydroxyphenyl)-(diisopropoxyphosphoryl)methyl)amino)-N-ethyl-N,N-dimethylpropan-1-aminium bromide (10b). Yield: 0.13 g (95%), mp: 99–101 °C. IR (cm^{-1}): 1026 (POC), 1247 (PO), 1655 (arom), 3621 (OH). ^1H NMR (CD_3OD) δ 0.98 (d, $^3J_{\text{HH}} = 6.1$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.26 (d, $^3J_{\text{HH}} = 6.1$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.32 (d, $^3J_{\text{HH}} = 6.2$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.35 (d, $^3J_{\text{HH}} = 6.1$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.38 (t, $^3J_{\text{HH}} = 7.4$ Hz, 3H, $\text{N}^+\text{CH}_2\text{CH}_3$), 1.47 (s, 18H, *t*-Bu), 1.94 (m, 2H, $\text{NHCH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.69 (m, 2H, NHCH_2), 3.01 (s, 6H, N^+CH_3), 3.34 (m, 2H, N^+CH_2), 3.45 (q, $^3J_{\text{HH}} = 7.4$ Hz, 2H, $\text{N}^+\text{CH}_2\text{CH}_3$), 3.95 (d, $^2J_{\text{PH}} = 19.8$ Hz, 1H, CH), 4.42 (m, 1H, OCH), 4.69 (m, 1H, OCH), 4.78 (br.s., 1H, OH), 7.26 (d, $^4J_{\text{PH}} = 2.0$ Hz, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 9.4 ($\text{N}^+\text{CH}_2\text{CH}_3$), 25.2 (CH_3 , $J_{\text{PC}} = 4.7$ Hz), 25.3 (CH_3 , $J_{\text{PC}} = 2.9$ Hz), 25.4 (CH_3 , $J_{\text{PC}} = 3.7$ Hz), 24.5 (CH_3 , $J_{\text{PC}} = 3.8$ Hz), 24.6 ($\text{NHCH}_2\text{CH}_2\text{CH}_2\text{N}$), 31.7 ($\text{C}(\text{CH}_3)_3$), 36.4 ($\text{C}(\text{CH}_3)_3$), 46.5 (NHCH_2), 51.7 ($\text{N}^+(\text{CH}_3)_2$), 61.7 ($\text{N}^+\text{CH}_2\text{CH}_3$), 62.9 (CH, $J_{\text{PC}} = 157.1$ Hz), 64.1 (NCH_2), 73.4 (OCH, $J_{\text{PC}} = 7.7$ Hz), 74.0 (OCH, $J_{\text{PC}} = 5.6$ Hz), 127.4 (CH_{arom} , $J_{\text{PC}} = 6.7$ Hz), 128.4 (C_{aromCH} , $J_{\text{PC}} = 2.1$ Hz), 140.2 ($\text{C}_{\text{aromC}}(\text{CH}_3)_3$, $J_{\text{PC}} = 1.7$ Hz), 156.1 (C_{aromOH} , $J_{\text{PC}} = 3.0$ Hz). ^{31}P NMR (CD_3OD) δ 22.0. HRMS (MALDI): calcd for $\text{C}_{28}\text{H}_{54}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 513, found 513. Anal. calcd for $\text{C}_{28}\text{H}_{54}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 56.65; H, 9.17; Br, 13.46; N, 4.72; P, 5.22. Found (%): C, 56.69; H, 9.13; Br, 13.51; N, 4.70; P, 5.18.

4.1.4.5 N-(2-(((3,5-Di-tert-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)ethyl)-N,N-dimethyldodecan-1-aminium bromide (11a). Yield: 0.15 g (98%), mp: 48–50 °C. IR (cm^{-1}): 1031 (POC), 1186 (PO), 1631 (arom), 3203 (NH), 3641 (OH). ^1H NMR (CD_3OD) δ 0.92 (t, $^3J_{\text{HH}} = 6.8$ Hz, 3H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$), 1.13 (t, $^3J_{\text{HH}} = 7.0$ Hz, 3H, OCH_2CH_3), 1.31 (t, $^3J_{\text{HH}} = 7.0$ Hz, 3H, OCH_2CH_3), 1.35 (m, 14H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$), 1.46 (s, 18H, *t*-Bu), 1.74 (m, 2H, $\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$), 3.01 (m, 2H, NHCH_2), 3.14 (s, 3H, N^+CH_3), 3.15 (s, 3H, N^+CH_3), 3.40 (m, 4H, $\text{NHCH}_2\text{CH}_2\text{N}^+$,

$\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_7\text{CH}_3$), 3.93 (m, 4H, OCH_2), 4.09 (d, $^2J_{\text{PH}} = 19.6$ Hz, 1H, CH), 7.26 (d, $^4J_{\text{PH}} = 2.0$ Hz, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 13.0 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 15.2 (OCH_2CH_3), 15.3 (OCH_2CH_3), 15.4 (OCH_2CH_3), 15.5 (OCH_2CH_3), 22.2 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 22.3 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 26.0 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 28.8 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_5\text{CH}_2\text{CH}_3$), 28.98 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 29.2 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 29.4 ($\text{C}(\text{CH}_3)_3$), 31.6 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 34.3 ($\text{C}(\text{CH}_3)_3$), 41.5 (NHCH_2), 41.6 (NHCH_2), 50.9 ($\text{N}^+(\text{CH}_3)_2$), 59.8 (CH, $J_{\text{PC}} = 156.9$ Hz), 62.2 (NCH_2), 62.6 (OCH_2 , $J_{\text{PC}} = 7.5$ Hz), 63.0 (OCH_2 , $J_{\text{PC}} = 7.2$ Hz), 64.9 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 125.0 ($\text{C}_{\text{arom}}\text{CH}$), 125.2 (CH_{arom}), 138.9 ($\text{C}_{\text{arom}}-\text{C}(\text{CH}_3)_3$), 154.2 ($\text{C}_{\text{arom}}\text{OH}$). ^{31}P NMR (CD_3OD) δ 24.2. HRMS (MALDI): calcd for $\text{C}_{33}\text{H}_{64}\text{N}_2\text{O}_4\text{P}$ [$\text{M} - \text{Br}$] $^+$ 584, found 584. Anal. calcd for $\text{C}_{33}\text{H}_{64}\text{BrN}_2\text{O}_4\text{P}$ (%): C 59.71; H 9.72; Br 12.04; N 4.22; P 4.67. Found (%): C 59.76; H 9.77; Br 11.90; N 4.19; P 4.69.

4.1.4.6 *N*-[2-(((3,5-Di-*tert*-butyl-4-hydroxyphenyl)-*(diisopropoxyphosphoryl)methyl*)amino)ethyl]-*N,N*-dimethyl-decan-1-aminium bromide (**11b**). Yield: 0.15 g (94%), mp: 80–83 °C. IR (cm⁻¹): 1026 (POC), 1298 (PO), 1660 (arom), 3408 (NH). ¹H NMR (CD₃OD) δ 0.92 (t, ³J_{HH} = 6.9 Hz, 3H, N⁺CH₂CH₂(CH₂)₇CH₃), 0.96 (d, ³J_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.25 (d, ³J_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.31 (d, ³J_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.32 (m, 14H, N⁺CH₂CH₂(CH₂)₇CH₃), 1.33 (d, ³J_{HH} = 6.1 Hz, 3H, OCH(CH₃)₂), 1.46 (s, 18H, *t*-Bu), 1.73 (m, 2H, N⁺CH₂CH₂(CH₂)₇CH₃), 3.01 (m, 2H, NHCH₂), 3.14 (s, 6H, N⁺CH₃), 3.36 (m, 2H, N⁺CH₂CH₂(CH₂)₇CH₃), 3.43 (m, 2H, N⁺CH₂), 3.99 (d, ²J_{PH} = 19.7 Hz, 1H, CH), 4.41 (m, 1H, OCH), 4.66 (m, 1H, OCH), 7.27 (d, ⁴J_{PH} = 2.0 Hz, 2H, H_{arom}). ¹³C NMR (CD₃OD) δ 13.0 (N⁺CH₂CH₂(CH₂)₆CH₂CH₃), 22.2 (N⁺CH₂CH₂(CH₂)₆CH₂CH₃), 22.4 (OCH(CH₃)₂), 22.9 (OCH(CH₃)₂), 23.0 (OCH(CH₃)₂), 23.1 (OCH(CH₃)₂), 26.1 (N⁺CH₂CH₂(CH₂)₆CH₂CH₃), 28.8 (N⁺CH₂CH₂CH₂(CH₂)₅CH₂CH₃), 28.9 (N⁺CH₂CH₂CH₂(CH₂)₄CH₂CH₂CH₃), 29.2 (N⁺CH₂CH₂CH₂(CH₂)₄CH₂CH₂CH₃), 29.4 (C(CH₃)₃), 31.6 (N⁺CH₂CH₂CH₂(CH₂)₄CH₂CH₂CH₃), 34.3 (C(CH₃)₃), 41.7 (NHCH₂), 50.9 (N⁺(CH₃)₂), 60.5 (CH, J_{PC} = 159.3 Hz), 62.2 (NCH₂), 64.9 (N⁺CH₂CH₂CH₂(CH₂)₄CH₂CH₂CH₃), 71.2 (OCH, J_{PC} = 7.8 Hz), 72.1 (OCH, J_{PC} = 7.6 Hz), 125.3 (C_{arom}CH, J_{PC} = 2.4 Hz), 125.6 (CH_{arom}, J_{PC} = 6.7 Hz), 138.1 (C_{arom}-C(CH₃)₃), 154.1 (C_{arom}OH, J_{PC} = 3.0 Hz). ³¹P NMR (CD₃OD) δ 22.5. HRMS (MALDI): calcd for C₃₅H₆₈N₂O₄P [M - Br]⁺ 612, found 612. Anal. calcd for C₃₅H₆₈BrN₂O₄P (%): C, 60.77; H, 9.91; Br, 11.55; N, 4.05; P, 4.48. Found (%): C, 60.82; H, 9.97; Br, 11.49; N, 4.09; P, 4.50.

4.1.4.7 *N*-[3-(((3,5-Di-*tert*-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)propyl]-*N,N*-dimethyldecan-1-aminium bromide (**12a**). Yield: 0.14 g (90%), mp: 76–78 °C. IR (cm⁻¹): 1051 (POC), 1656 (arom), 3394 (NH). ¹H NMR (CD₃OD) δ 0.87 (t, ³J_{HH} = 6.5 Hz, 3H, N⁺CH₂CH₂(CH₂)₇CH₃), 1.06 (t, ³J_{HH} = 7.00 Hz, 3H, OCH₂CH₃), 1.25–1.33 (m, 17H, N⁺CH₂CH₂(CH₂)₇CH₃, OCH₂CH₃), 1.42 (s, 18H, *t*-Bu), 1.68 (m, 2H, N⁺CH₂CH₂(CH₂)₇CH₃), 1.88 (m, 2H, NHCH₂CH₂CH₂N⁺), 2.69 (br.t., ³J_{HH} = 5.3 Hz, 2H, NHCH₂), 3.35 (s, 3H, NCH₃), 3.36 (s, 3H, NCH₃), 3.50–3.60 (m, 4H, N⁺CH₂, N⁺CH₂CH₂(CH₂)₇CH₃), 3.70 (m, 1H, OCH₂), 3.89 (m, 1H,

OCH_2), 4.02 (m, 2H, OCH_2), 3.81 (d, $^2J_{\text{PH}} = 19.24$ Hz, 1H, CH), 5.21 (s, 1H, OH), 7.12 (s, 2H, H_{arom}). ^{13}C NMR (CD_3OD) δ 14.0 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{C}\equiv\text{CH}$), 16.2 ($\text{OCH}_2\text{C}\equiv\text{CH}$), 16.5 ($\text{OCH}_2\text{C}\equiv\text{CH}$), 22.6 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 22.8 ($\text{N}^+\text{CH}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 23.4 ($\text{NHCH}_2\text{C}\equiv\text{CH}_2\text{CH}_2\text{N}^+$), 26.2 ($\text{N}^+\text{CH}_2\text{C}\equiv\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{CH}_3$), 29.1 ($\text{N}^+\text{CH}_2\text{CH}_2\text{C}\equiv\text{CH}_2(\text{CH}_2)_5\text{CH}_2\text{CH}_3$), 29.2 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 29.4 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 30.3 ($\text{C}(\text{C}\equiv\text{CH}_3)_3$), 31.8 ($\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 34.3 ($\text{C}(\text{C}\equiv\text{CH}_3)_3$), 44.5 (NHCH_2), 44.6 (NHCH_2), 51.3 ($\text{N}^+(\text{CH}_3)_2$), 60.9 (CH, $J_{\text{PC}} = 154.9$ Hz), 62.3 (OCH_2 , $J_{\text{PC}} = 7.4$ Hz), 62.5 (NCH_2), 62.9 (OCH_2 , $J_{\text{PC}} = 7.1$ Hz), 64.5 ($\text{N}^+\text{C}\equiv\text{CH}_2\text{CH}_2\text{CH}_2(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CH}_3$), 124.9 (CH_{arom} , $J_{\text{PC}} = 6.4$ Hz), 125.9 ($\text{C}_{\text{arom}}\text{CH}$, $J_{\text{PC}} = 3.2$ Hz), 138.1 ($\text{C}_{\text{arom}}\text{-C}(\text{CH}_3)_3$, $J_{\text{PC}} = 2.1$ Hz), 153.7 ($\text{C}_{\text{arom}}\text{OH}$, $J_{\text{PC}} = 3.2$ Hz). ^{31}P NMR (CD_3OD) δ 22.7. HRMS [MALDI]: calcd for $\text{C}_{34}\text{H}_{66}\text{N}_2\text{O}_4\text{P}$ [$\text{M} - \text{Br}$] $^+$ 597, found 597. Anal. calcd for $\text{C}_{34}\text{H}_{66}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 60.25; H, 9.82; Br, 11.79; N, 4.13; P, 4.57. Found (%): C, 60.31; H, 9.89; Br, 11.68; N, 4.06; P, 4.51.

4.1.4.8 *N*-(3-(((3,5-Di-*tert*-butyl-4-hydroxyphenyl)-
(diisopropoxyphosphoryl)methyl)amino)propyl)-*N,N*-dimethyl-
decan-1-aminium bromide (**12b**). Yield: 0.15 g (92%), mp: 38–
40 °C. IR (cm⁻¹): 1031 (POC), 1294 (PO), 1658 (arom), 3400
(NH). ¹H NMR (CD₃OD) δ 0.92 (t, ³J_{HH} = 6.9 Hz, 3H,
N⁺CH₂CH₂(CH₂)₇CH₃), 0.97 (d, ³J_{HH} = 6.2 Hz, 3H,
OCH(CH₃)₂), 1.25 (d, ³J_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.30 (d,
³J_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.32 (m, 14H,
N⁺CH₂CH₂(CH₂)₇CH₃), 1.33 (d, ³J_{HH} = 6.1 Hz, 3H,
OCH(CH₃)₂), 1.45 (s, 18H, *t*-Bu), 1.73 (m, 2H,
N⁺CH₂CH₂(CH₂)₇CH₃), 1.90 (m, 2H, NHCH₂CH₂CH₂N⁺), 2.66
(m, 2H, NHCH₂), 3.06 (s, 3H, NCH₃), 3.07 (s, 3H, NCH₃),
3.28–3.41 (m, 4H, N⁺CH₂, N⁺CH₂CH₂(CH₂)₇CH₃), 3.91 (d, ²J_{PH}
= 19.6 Hz, 1H, CH), 4.40 (m, 1H, OCH), 4.66 (m, 1H, OCH),
7.23 (d, ⁴J_{PH} = 2.1 Hz, 2H, H_{arom}). ³¹P NMR (CD₃OD) δ 24.2.
HRMS (MALDI): calcd for C₃₆H₇₀N₂O₄P [M – Br]⁺ 626, found
626. Anal. calcd for C₃₆H₇₀BrN₂O₄P (%): C, 61.26; H, 10.00;
Br, 11.32; N, 3.97; P, 4.39. Found (%): C, 61.21; H, 10.11; Br,
11.27; N, 3.94; P, 4.43.

4.1.4.9 *N*-[2-(((3,5-*Di-tert-butyl-4-hydroxyphenyl*)-(diethoxyphosphoryl)methyl)amino)ethyl]-*N,N*-dimethyldodecan-1-aminium bromide (**13a**). Yield: 0.14 g (88%), mp: 45–47 °C. IR (cm⁻¹): 1027 (POC), 1176 (PO), 1634 (arom), 3221 (NH), 3637 (OH). ¹H NMR (CD₃OD) δ 0.88 (t, ³J_{HH} = 6.7 Hz, 3H, N⁺CH₂CH₂(CH₂)₉CH₃), 1.07 (t, ³J_{HH} = 7.05 Hz, 3H, OCH₂CH₃), 1.26 (m, 21H, N⁺CH₂CH₂(CH₂)₉CH₃, OCH₂CH₃), 1.43 (s, 18H, *t*-Bu), 1.68 (m, 2H, N⁺CH₂CH₂(CH₂)₉CH₃), 3.10 (m, 2H, NHCH₂), 3.41 (s, 6H, NCH₃), 3.42 (s, 6H, NCH₃), 3.58 (m, 2H, N⁺CH₂CH₂(CH₂)₉CH₃), 3.69–3.94 (m, 3H, OCH₂, CH), 4.03 (m, 2H, OCH₂), 5.24 (s, 1H, CH), 7.16 (d, ⁴J_{PH} = 2.03 Hz, 2H, H_{arom}). ¹³C NMR (CD₃OD) δ 14.1 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 16.2 (OCH₂CH₃), 16.3 (OCH₂CH₃), 16.4 (OCH₂CH₃), 16.5 (OCH₂CH₃), 22.6 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 22.9 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 26.3 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 29.2 (N⁺CH₂CH₂CH₂(CH₂)₇CH₂CH₃), 29.3 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃), 29.4 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃), 29.5 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃), 29.6 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃), 30.3 (C(CH₃)₃), 31.9 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃).

(CH₂)₆CH₂CH₂CH₃), 34.3 (C(CH₃)₃), 42.6 (NHCH₂), 42.7 (NHCH₂), 51.8 (N⁺(CH₃)₂), 60.6 (CH, *J*_{PC} = 157.0 Hz), 62.2 (NCH₂), 62.3 (OCH₂, *J*_{PC} = 7.5 Hz), 62.8 (OCH₂, *J*_{PC} = 7.2 Hz), 65.3 (N⁺CH₂(CH₂)₁₀CH₃), 125.1 (C_{arom}CH), 125.2 (CH_{arom}), 136.2 (C_{arom}-C(CH₃)₃), 153.9 (C_{arom}OH). ³¹P NMR (CD₃OD) δ 24.2. HRMS (MALDI): calcd for C₃₅H₆₈N₂O₄P [M - Br]⁺ 612, found 612. Anal. calcd for C₃₅H₆₈BrN₂O₄P (%): C, 60.77; H, 9.91; Br, 11.55; N, 4.05; P, 4.48. Found (%): C, 60.71; H, 9.98; Br, 11.49; N, 4.00; P, 4.52.

4.1.4.10 *N*-(3-(((3,5-Di-*tert*-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)propyl)-*N,N*-dimethyldodecan-1-aminium bromide (**14a**). Yield: 0.15 g (93%), mp: 46–48 °C. IR (cm⁻¹): 1024 (POC), 1649 (arom), 3398 (NH). ¹H NMR (CD₃OD) δ 0.86 (t, ³*J*_{HH} = 6.6 Hz, 3H, N⁺CH₂CH₂(CH₂)₉CH₃), 1.05 (t, ³*J*_{HH} = 7.0 Hz, 3H, OCH₂CH₃), 1.16–1.36 (m, 21H, N⁺CH₂CH₂(CH₂)₉CH₃, OCH₂CH₃), 1.41 (s, 18H, *t*-Bu), 1.68 (m, 2H, N⁺CH₂CH₂(CH₂)₉CH₃), 1.88 (m, 2H, NHCH₂CH₂CH₂N⁺), 2.68 (t, ³*J*_{HH} = 5.9 Hz, 2H, NHCH₂), 3.33 (s, 3H, NCH₃), 3.34 (s, 3H, NCH₃), 3.49–3.59 (m, 4H, N⁺CH₂, N⁺CH₂CH₂(CH₂)₉CH₃), 3.66–3.72 (m, 1H, OCH₂), 3.85–3.90 (m, 1H, OCH₂), 3.98–4.04 (m, 2H, OCH₂), 3.81 (d, ²*J*_{PH} = 19.3 Hz, 1H, CH), 5.20 (s, 1H, CH), 7.12 (s, 2H, H_{arom}). ¹³C NMR (CD₃OD) δ 14.1 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 16.2 (OCH₂CH₃), 16.3 (OCH₂CH₃), 16.5 (OCH₂CH₃), 22.6 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 22.8 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 23.4 (NHCH₂CH₂CH₂N⁺), 26.2 (N⁺CH₂CH₂(CH₂)₈CH₂CH₃), 29.2 (N⁺CH₂CH₂CH₂(CH₂)₇CH₂CH₃), 29.4 (N⁺CH₂CH₂CH₂(CH₂)₆CH₂CH₂CH₃), 29.3, 29.4, 29.5, 29.6 (N⁺CH₂CH₂CH₂(CH₂)₄CH₂CH₂CH₃), 30.3 (C(CH₃)₃), 34.3 (C(CH₃)₃), 44.6 (NHCH₂), 44.7 (NHCH₂), 51.3 (N⁺(CH₃)₂), 60.9 (CH, *J*_{PC} = 154.8 Hz), 62.3 (OCH₂, *J*_{PC} = 7.4 Hz), 62.4 (NCH₂), 62.9 (OCH₂, *J*_{PC} = 7.2 Hz), 64.4 (N⁺CH₂(CH₂)₁₀CH₃), 124.9 (CH_{arom}, *J*_{PC} = 6.1 Hz), 125.9 (C_{arom}CH), 136.1 (C_{arom}-C(CH₃)₃), 153.6 (C_{arom}OH, *J*_{PC} = 2.8 Hz). ³¹P NMR (CD₃OD) δ 22.7. HRMS (MALDI): calcd for C₃₆H₇₀N₂O₄P [M - Br]⁺ 626, found 626. Anal. calcd for C₃₆H₇₀BrN₂O₄P (%): C, 61.26; H, 10.00; Br, 11.32; N, 3.97; P, 4.39. Found (%): C, 61.31; H, 10.06; Br, 11.37; N, 3.92; P, 4.30.

4.1.4.11 *N*-Benzyl-2-(((3,5-di-*tert*-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)-*N,N*-dimethylethan-1-aminium bromide (**15a**).

Yield: 0.14 g (99%), mp: 100–102 °C. IR (cm⁻¹): 1030 (POC), 1216 (PO), 1626 (arom), 3418 (NH). ¹H NMR (CD₃OD) δ 1.11 (t, ³*J*_{HH} = 7.0 Hz, 3H, OCH₂CH₃), 1.28 (t, ³*J*_{HH} = 7.0 Hz, 3H, OCH₂CH₃), 1.45 (s, 18H, *t*-Bu), 3.11 (m, 2H, NHCH₂), 3.12 (s, 3H, N⁺CH₃), 3.13 (s, 3H, N⁺CH₃), 3.49 (m, 2H, N⁺CH₂), 3.79

(m, 1H, OCH₂CH₃), 3.92 (m, 1H, OCH₂CH₃), 4.08 (m, 2H, OCH₂CH₃), 4.11 (d, ²*J*_{PH} = 20.0 Hz, 1H, CH), 4.64 (s, 2H, CH₂-Ph), 7.27 (d, ⁴*J*_{PH} = 1.7 Hz, 2H, H_{arom}), 7.57 (m, 5H, CH₂Ph). ¹³C NMR (CD₃OD) δ 15.2 (OCH₂CH₃), 15.3 (OCH₂CH₃), 15.4 (OCH₂CH₃), 29.4 (C6), 34.3 (C5), 41.6 (C8), 41.7 (C8), 49.8 (C10), 59.7 (C7, *J*_{PC} = 157.5 Hz), 62.5 (OCH₂, *J*_{PC} = 7.5 Hz), 63.0 (OCH₂, *J*_{PC} = 7.3 Hz), 63.2 (C9), 68.8 (C11), 125.0 (C3, *J*_{PC} = 6.5 Hz), 125.3 (C4, *J*_{PC} = 2.3 Hz), 127.6 (C12), 128.9 (C14), 130.5 (C15), 132.9 (C13), 138.2 (C2, *J*_{PC} = 2.2 Hz), 154.2 (C1, *J*_{PC} = 3.2 Hz). ³¹P NMR (CD₃OD) δ 24.3. HRMS (MALDI): calcd for C₃₀H₅₀N₂O₄P [M - Br]⁺ 533, found 533. Anal. calcd for C₃₀H₅₀BrN₂O₄P (%): C, 58.72; H, 8.21; Br, 13.02; N, 4.57; P, 5.05. Found (%): C, 58.55; H, 8.74; Br, 12.85; N, 4.24; P, 4.71.

4.1.4.12 *N*-Benzyl-2-(((3,5-di-*tert*-butyl-4-hydroxyphenyl)-(diisopropoxyphosphoryl)methyl)amino)-*N,N*-dimethylethan-1-aminium bromide (**15b**). Yield: 0.14 g (93%), mp: 151–153 °C. IR (cm⁻¹): 1029 (POC), 1214 (PO), 1624 (arom), 3425 (NH). ¹H NMR (CD₃OD) δ 0.92 (d, ³*J*_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.24 (d, ³*J*_{HH} = 6.2 Hz, 3H, OCH(CH₃)₂), 1.28 (d, ³*J*_{HH} = 5.9 Hz, 3H, OCH(CH₃)₂), 1.29 (d, ³*J*_{HH} = 5.9 Hz, 3H, OCH(CH₃)₂), 1.45 (s, 18H, *t*-Bu), 3.07 (m, 2H, NHCH₂), 3.11 (s, 3H, N⁺CH₃), 3.12 (s, 3H, N⁺CH₃), 3.47 (m, 2H, N⁺CH₂), 4.02 (d, ²*J*_{PH} = 20.4 Hz, 1H, CH), 4.38 (m, 1H, OCH(CH₃)₂), 4.63 (s, 1H, CH₂Ph), 4.64 (s, 1H, CH₂Ph), 4.65 (m, 1H, OCH(CH₃)₂), 7.26 (d, ⁴*J*_{PH} = 2.0 Hz, 2H, H_{arom}), 7.54 (m, 5H, CH₂Ph). ³¹P NMR (CD₃OD) δ 22.7. HRMS (MALDI): calcd for C₃₂H₅₄N₂O₄P [M - Br]⁺ 562, found 562. Anal. calcd for C₃₂H₅₄BrN₂O₄P (%): C, 59.90; H, 8.48; Br, 12.45; N, 4.37; P, 4.83. Found (%): C, 59.95; H, 8.52; Br, 12.41; N, 4.39; P, 4.80.

4.1.4.13 *N*-Benzyl-3-(((3,5-di-*tert*-butyl-4-hydroxyphenyl)-(diethoxyphosphoryl)methyl)amino)-*N,N*-dimethylpropan-1-aminium bromide (**16a**).

Yield: 0.13 g (90%), mp: 97–99 °C. IR (cm⁻¹): 1027 (POC), 1219 (PO), 1632 (arom), 3401 (NH). ¹H NMR (CD₃OD) δ 1.14 (t, ³*J*_{HH} = 7.2 Hz, 3H, OCH₂CH₃), 1.31 (t, ³*J*_{HH} = 7.1 Hz, 3H, OCH₂CH₃), 1.46 (s, 18H, *t*-Bu), 2.08 (m, 2H, NHCH₂CH₂CH₂N⁺), 2.69 (m, 2H, NHCH₂), 3.07 (s, 6H, N⁺CH₃), 3.34 (m, 2H, N⁺CH₂), 3.57 (s, 2H, CH₂Ph), 3.86 (m, 1H, OCH₂CH₃), 3.95 (m, 1H, OCH₂CH₃), 4.08 (m, 2H, OCH₂CH₃), 4.06 (d, ²*J*_{PH} = 21.4 Hz, 1H, CH), 7.26 (d, ⁴*J*_{PH} = 2.2 Hz, 2H, H_{arom}), 7.53 (t, ³*J*_{HH} = 6.7 Hz, 2H, H15), 7.57 (t, ³*J*_{HH} = 6.7 Hz, 1H, H16), 7.60 (d, ³*J*_{HH} = 6.7 Hz, 2H, H14). ¹³C NMR (CD₃OD) δ 17.6 (OCH₂CH₃), 17.7 (OCH₂CH₃), 24.9 (C9), 31.7 (C6), 36.5 (C5), 46.4 (C8), 51.6 (C11), 62.4 (C7, *J*_{PC} = 155.3 Hz), 64.8 (OCH₂, *J*_{PC} = 7.2 Hz), 65.0 (C10), 65.3 (OCH₂,

$J_{\text{PC}} = 10.8$ Hz), 69.6 (C12), 127.2 (C3, $J_{\text{PC}} = 6.5$ Hz), 128.0 (C4, $J_{\text{PC}} = 2.6$ Hz), 129.8 (C13), 131.3 (C15), 132.8 (C16), 135.0 (C14), 140.4 (C2, $J_{\text{PC}} = 1.8$ Hz), 156.3 (C1, $J_{\text{PC}} = 3.1$ Hz). ^{31}P NMR (CD_3OD) δ 24.6. HRMS (MALDI): calcd for $\text{C}_{31}\text{H}_{52}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 547, found 547. Anal. calcd for $\text{C}_{31}\text{H}_{52}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 59.32; H, 8.35; Br, 12.73; N, 4.46; P, 4.93. Found (%): C, 58.97; H, 8.81; Br, 12.04; N, 4.14; P, 4.21.

4.1.4.14 N-Benzyl-3-(((3,5-di-tert-butyl-4-hydroxyphenyl)-(diisopropoxyphosphoryl)methyl)amino)-N,N-dimethylpropan-1-aminium bromide (16b). Yield: 0.14 g (93%), mp: 146–148 °C. IR (cm^{-1}): 1033 (POC), 1221 (PO), 1629 (arom), 3416 (NH). ^1H NMR (CD_3OD) δ 0.96 (d, $^3J_{\text{HH}} = 6.2$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.25 (d, $^3J_{\text{HH}} = 6.2$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.29 (d, $^3J_{\text{HH}} = 5.8$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.31 (d, $^3J_{\text{HH}} = 5.6$ Hz, 3H, $\text{OCH}(\text{CH}_3)_2$), 1.45 (s, 18H, *t*-Bu), 2.06 (m, 2H, $\text{NHCH}_2\text{CH}_2\text{CH}_2\text{N}^+$), 2.69 (m, 2H, NHCH_2), 3.05 (s, 6H, N^+CH_3), 3.41 (m, 2H, N^+CH_2), 3.94 (d, $^2J_{\text{PH}} = 19.6$ Hz, 1H, CH), 4.41 (m, 1H, $\text{OCH}(\text{CH}_3)_2$), 4.55 (s, 2H, CH_2Ph), 4.67 (m, 1H, $\text{OCH}(\text{CH}_3)_2$), 7.24 (d, $^4J_{\text{PH}} = 1.9$ Hz, 2H, H_{arom}), 7.56 (m, 5H, CH_2Ph). ^{13}C NMR (CD_3OD) δ 22.4 ($\text{OCH}(\text{CH}_3)_2$), 22.7 (C9), 23.0 ($\text{OCH}(\text{CH}_3)_2$), 23.1 ($\text{OCH}(\text{CH}_3)_2$), 23.2 ($\text{OCH}(\text{CH}_3)_2$), 29.5 (C6), 34.3 (C5), 44.3 (C8), 49.3 (C11), 60.8 (C7, $J_{\text{PC}} = 157.1$ Hz), 62.7 (C10), 67.3 (C12), 71.3 (OCH , $J_{\text{PC}} = 7.2$ Hz), 71.9 (OCH , $J_{\text{PC}} = 10.8$ Hz), 125.2 (C3, $J_{\text{PC}} = 6.7$ Hz), 126.2 (C4, $J_{\text{PC}} = 2.8$ Hz), 127.5 (C13), 129.0 (C15), 130.5 (C16), 132.8 (C14), 138.0 (C2, $J_{\text{PC}} = 2.2$ Hz), 153.9 (C1, $J_{\text{PC}} = 3.1$ Hz). ^{31}P NMR (CD_3OD) δ 22.9. HRMS (MALDI): calcd for $\text{C}_{33}\text{H}_{56}\text{N}_2\text{O}_4\text{P}$ $[\text{M} - \text{Br}]^+$ 575, found 575. Anal. calcd for $\text{C}_{33}\text{H}_{56}\text{BrN}_2\text{O}_4\text{P}$ (%): C, 60.45; H, 8.61; Br, 12.19; N, 4.27; P, 4.72. Found (%): C, 60.50; H, 8.66; Br, 12.14; N, 4.25; P, 4.76.

Conflicts of interest

There are no conflicts to declare.

References

- 1 M. Steiner, R. Landolfi, N. C. Motola and J. G. Turcotte, *Biochem. Biophys. Res. Commun.*, 1985, **133**(3), 851–855.
- 2 V. M. Golubovskaya, C. Nyberg, M. Zheng, F. Kweh, A. Magis, D. Ostrov and W. G. Cance, *J. Med. Chem.*, 2008, **51**(23), 7405–7416.
- 3 A. V. Bogdanov, T. A. Kutuzova and V. F. Mironov, *Russ. J. Gen. Chem.*, 2016, **86**(3), 756–757.
- 4 E. A. Chugunova, N. I. Akyzbekov, N. O. Appazov, E. M. Makhrus and A. R. Burilov, *Russ. J. Org. Chem.*, 2016, **52**(6), 920–921.
- 5 V. E. Semenov, A. D. Voloshina and N. V. Kulik, *et al.*, *Russ. Chem. Bull.*, 2015, **64**(12), 2885–2896.
- 6 A. Kouadri-Boudjelthia and J. M. Wallach, *Int. J. Biochem. Cell Biol.*, 1997, **29**(2), 353–359.
- 7 F. C. Krebs, S. R. Miller, D. Malamud, M. K. Howett and B. Wigdahl, *Antiviral Res.*, 1999, **43**, 157–173.
- 8 L. Belec, C. Tevi-Benissan, A. Bianchi, S. Cotigny, M. Beumont-Mauviel, A. Si-Mohamed and J.-E. Malkin, *J. Antimicrob. Chemother.*, 2000, **46**, 685–693.
- 9 D. L. Patton, S. K. Wang and C. C. Kuo, *Antimicrob. Agents Chemother.*, 1992, **36**, 1478–1482.
- 10 D. B. Vieira and A. M. Carmona-Ribeiro, *J. Antimicrob. Chemother.*, 2006, **58**, 760–767.
- 11 M. R. Salton, R. W. Horne and V. E. Cosslett, *J. Gen. Microbiol.*, 1951, **5**, 405–407.
- 12 C. J. Ioannou, G. W. Hanlon and S. P. Denyer, *Antimicrob. Agents Chemother.*, 2007, **51**, 296–306.
- 13 A. H. Fairlamb, N. A. R. Gow and K. R. Matthews, *et al.*, *Nat. Microbiol.*, 2016, **1**(7), 1–14.
- 14 G. Aysel, I. Taylan, T. Nalan and O. Gulten, *Turk. J. Pharm. Sci.*, 2005, **2**, 1–10.
- 15 M. Aránzazu Partearroyo, H. Ostolaza, F. M. Goñi and E. Barberá-Guillem, *Biochem. Pharmacol.*, 1990, **40**, 1323–1328.
- 16 K. S. Warren, *J. Clin. Invest.*, 1958, **37**(4), 497–501.
- 17 Yu. N. Oludina, S. V. Bukharov and R. G. Tagasheva, *et al.*, *Pharm. Chem. J.*, 2014, **48**(1), 5–7.
- 18 D. V. Arefev, Sintez kovalentnyh kon'ugatov dextranov – prostranstvenno-zatruneinye fenoly i izucheniye ih anti-radikalnoi aktivnosti: Avtoref. ... dis. kand. him. nauk: 02.00.06. — SPb., 2000, p. 24.
- 19 Y. Isomura, N. Ito, H. Homma, T. Abe and K. Kubo, *Chem. Pharm. Bull.*, 1983, **31**(9), 3168–3178.
- 20 S. Rollas and K. Güniz, *Molecules*, 2007, **12**(6), 1910–1939.
- 21 R. Vachy, B. Wichrowski and S. A. Fileco, Pat. EP0557404B1, France. Utilisation de composés 2,6-di-tert-butylphenols substitués en position 4 dans le traitement et la prévention du sida, 1996, p. 20.
- 22 R. A. Scherrer, Pat. US5237070, USA. Substituted di-tert-butylphenols, Riker Lab. Inc., 1993, p. 15.
- 23 I. Galkina, Yu. Bakhtiyarova, V. Andriyashin, V. Galkin and R. Cherkasov, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2013, **188**, 15–18.
- 24 Yu. N. Oludina, M. A. Sazykina and E. V. Prazdnova, *et al.*, *Pharm. Chem. J.*, 2015, **48**(12), 787–790.
- 25 G. A. Nikiforov, F. I. Braginskaya, V. V. Ershov and E. B. Burlakova, Pat. No 2029760. Soly N,N-dimetilaminoetil-β-(4-gidroksi-3,5-di-tretbutilfenil)propionate v kachestve inhibitora holinesterazy, 1995, p. 6.
- 26 E. Y. Parshina, A. B. Rubin and L. Y. Gendel, *Pharm. Chem. J.*, 2012, **46**(2), 82–85.
- 27 N. A. Antonova, M. N. Kolyada, V. P. Osipova, Yu. T. Pimenov, N. T. Berberova, V. Yu. Tyurin, Yu. A. Gracheva and E. R. Milaeva, *Dokl. Chem.*, 2008, **419**(1), 62–64.
- 28 E. T. Denisov and I. B. Afanas'ev, *Oxidation and Antioxidants in Organic Chemistry and Biology*, Taylor and Francis, Boca Raton, 2005.
- 29 B. P. Morgan, J. M. Scholtz, M. D. Ballinger, I. D. Zipkin and P. A. Bartlett, *J. Am. Chem. Soc.*, 1991, **113**, 297–307.
- 30 D. Y. Jackson, J. W. Jacobs, R. Sugawara, S. H. Reich, P. A. Bartlett and P. G. Schultz, *J. Am. Chem. Soc.*, 1988, **110**(14), 4841–4842.
- 31 P. H. Trung, N. L. Mong, N. Eric, G.-G. Yves and B. C. Leigh, Pat. EP0559079(A1). Substituted aminophosphonate derivatives, process for their preparation and pharmaceutical compositions containing them, Symphar S.A., 1993, p. 17.

- 32 W. Erhard, R. Erhard, T. Werner, R. Ruth and W. K. Ulrich, Pat. EP 703239(A1), Aminomethylphosphonic and aminomethylphosphinic acids derivatives and their use in the treatment of degenerative articular diseases, 1996, p. 44.
- 33 P. Arde and R. V. Anand, *Org. Biomol. Chem.*, 2013, **00**, 1–6.
- 34 Yu. V. Bakhtiyarova, M. S. Bondar, V. V. Andriyashin, O. N. Kataeva, I. V. Galkina and V. I. Galkin, *Mendeleev Commun.*, 2009, **19**, 37–38.
- 35 B. Costisella, I. Keitel, H. Gross and K. Nadolski, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1994, **84**(1), 13–19.
- 36 R. K. Ismagilov, V. A. Moskva, T. V. Zyкова and V. P. Arkhipov, *Russ. J. Gen. Chem.*, 1994, **64**(9), 1472–1474.
- 37 E. M. Gibadullina, T. R. Shaekhov, A. K. Badrtdinov, Yu. K. Voronina and A. R. Burilov, *Russ. Chem. Bull.*, 2013, **62**(7), 1609–1613.
- 38 S. V. Bukharov, A. R. Burilov, Yu. N. Oludina, R. G. Tagasheva, V. V. Syakaev, R. Z. Musin and G. N. Nugumanova, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2016, **191**(7), 1069–1074.
- 39 M. B. Gazizov, A. L. Tarakanova, R. K. Ismagilov, L. P. Shamsutdinova, R. F. Karimova and R. N. Burangulova, *Russ. J. Gen. Chem.*, 2016, **86**(2), 326–330.
- 40 Yu. N. Oludina, S. V. Bukharov, A. R. Burilov, R. G. Tagasheva, V. V. Syakaev, R. Z. Musin, E. F. Akhmetova and G. N. Nugumanova, *Russ. Chem. Bull.*, 2014, **63**(1), 115–117.
- 41 L. I. Vagapova, L. R. Amirova, A. R. Burilov, M. A. Pudovik and O. G. Sinyashin, *Russ. J. Org. Chem.*, 2015, **51**(9), 1294–1297.
- 42 L. I. Vagapova, L. R. Amirova, V. V. Syakaev, J. K. Voronina, D. B. Krivolapov, A. R. Burilov, M. A. Pudovik and O. G. Sinyashin, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2015, **190**, 2283–2290.
- 43 D. V. Aref'ev, I. S. Belostotskaya, V. B. Vol'eva, N. S. Domnina, O. Yu. Sergeeva, N. L. Komissarova, O. Yu. Sergeeva and R. S. Khrustaleva, *Russ. Chem. Bull.*, 2007, **56**(4), 781–790.
- 44 R. G. Tagasheva, E. R. Shakirova, S. V. Bukharov, I. V. Galkina, G. K. Ziyatdinova, R. Z. Musin and I. Kh. Rizvanov, *Russ. J. Gen. Chem.*, 2018, **88**(1), 68–72.
- 45 R. R. Azmukhanova, E. M. Gibadullina, N. B. Pazilova, M. A. Pudovik and A. R. Burilov, *Russ. J. Org. Chem.*, 2017, **53**(11), 1746–1748.
- 46 V. E. Semenov, A. D. Voloshina, N. V. Kulik, A. S. Strobykina, R. K. Giniyatullin, L. F. Saifina, A. E. Nikolaev, E. S. Krylova, V. V. Zobov and V. S. Reznik, *Russ. Chem. Bull.*, 2015, **64**(12), 2885.
- 47 V. E. Semenov, A. S. Mikhailov, A. D. Voloshina, N. V. Kulik, A. D. Nikitashina, V. V. Zobov, S. V. Kharlamov, S. K. Latypov and V. S. Reznik, *Eur. J. Med. Chem.*, 2011, **46**, 4715.
- 48 D. A. Tatarinov, D. M. Kuznetsov, A. D. Voloshina, A. P. Lyubina, A. S. Strobykina, F. K. Mukhitova, F. M. Polyancev and V. F. Mironov, *Tetrahedron*, 2016, **72**, 8493.
- 49 A. D. Voloshina, V. E. Semenov, A. S. Strobykina, N. V. Kulik, E. S. Krylova, V. V. Zobov and V. S. Reznik, *Russ. J. Bioorg. Chem.*, 2017, **43**(2), 170–176.
- 50 A. V. Alekseev, E. V. Proskurnina and Y. A. Vladimirov, *Moscow Univ. Chem. Bull.*, 2012, **67**(3), 127–132.
- 51 A. Krasowska, D. Rosiak, K. Szkapiak and M. Lukaszewicz, *Curr. Top. Biophys.*, 2000, **24**(920), 89–95.