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Synthesis and Spectral Characterization of *N*-[2-(4-Halophenoxy)-3-(3-chlorophenyl)-3, 4-dihydro-2*H*-1,3,2-λ^5-benzoxazaphosphinin-2-yliden]-N-Substituted Amines by the Staudinger Reaction

C. Venkateswarlu,[1] P. V. V. Satyanarayana,[2] C. V. Nageswara Rao,[3] K. Reddy Mohan Naidu,[4] and C. Naga Raju[4]

[1]*Department of Chemistry, K. V. R. College, Nandigama 521 185, India*

[2]*Department of Chemistry, Acharya Nagarjuna University, Nagarjuna Nagar 522 510, India.*

[3]*P. G. Department of Chemistry, AG & SG Siddhartha College of Arts & Science, Vuyyuru 521 165, India*

[4]*Department of Chemistry, Sri Venkateswara University, Tirupati 517 502, India*

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ABSTRACT: *The synthesis of the title compounds was accomplished in four steps. The synthetic route involves the preparation of Schiff's base by reacting salicylaldehyde with* m-*chloroaniline in EtOH. The Schiff's base was then reduced with $NaBH_4$/MeOH. In the second step, PCl_3 was reacted with* p-*chlorophenol/*p-*bromophenol in THF in the presence of Et_3N to obtain P(III) dichloride derivatives. The reduced Schiff's base and dichloride derivatives were reacted in equimolar quantities in the presence of Et_3N in THF to get the cyclized product. Alkyl azides were prepared by reacting alkyl bromides with sodium azide, and then alkyl azides were treated with the cyclized product to obtain the title compounds. The structure of these novel compounds was elucidated by elemental analysis, IR, ^1H, ^{13}C, ^{31}P NMR, and mass spectroscopy.* © 2010 Wiley Periodicals, Inc. Heteroatom Chem 21:499–504, 2010; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.20639

Correspondence to: C. V. Nageswara Rao; e-mail: chavavnrao@gmail.com.

INTRODUCTION

Staudinger and Meyer [1] reported the first synthesis of phosphazo compounds in 1919 by the reaction of tertiary phosphines with organic azides. The Staudinger reaction, in its classical form, is a two-step process involving the initial electrophilic addition of an azide to a trivalent phosphorus center followed by nitrogen elimination from the intermediate phosphazide giving the iminophosphorane.

It has not attracted the attention of the chemists for about three to four decades after its discovery. The landmark discovery of the imination of phosphorus pentachloride and its derivatives by compounds containing the amino group by Kirsanov [2] initiated an extensive development of chemistry of phosphazo compounds and renewed the interest to the Staudinger reaction. They examined a variety of new oxidative imination reactions of trivalent phosphorus compounds producing phosphazo derivatives. A substantial contribution that extended the area of exploration and utilization of Staudinger reaction was made by Kabachnik et al. [3–5]. They demonstrated that besides the tertiary phosphines,

the esters of phosphorus acids may also be used for the preparation of phosphazo compounds, and this fact opened up new possibilities of the Staudinger reaction and prompted its application.

The phosphazo reaction is generally used for the synthesis of P-halogenated products. The Staudinger reaction, on the other hand, is more convenient for the synthesis of P-alkoxylated, P-thioalkylated, P-aroxylated, and P-aminated phosphazo compounds.

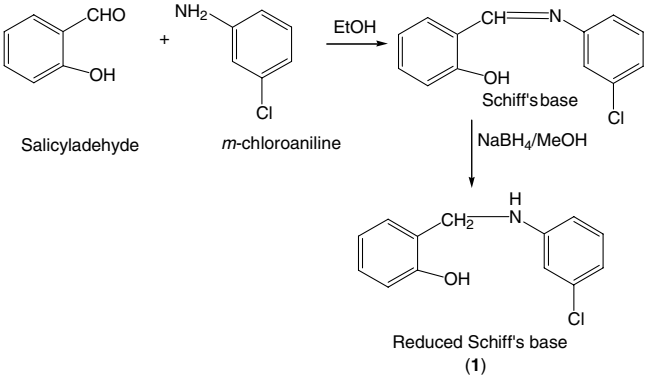
Iminophosphoranes play an important role in heterocyclic synthesis [6,7]. In few cases, the intermediate phosphazides have been isolated [8] or trapped via an intermolecular reaction [9]. But most of such phosphazides lose nitrogen at room temperature to give the corresponding iminophosphoranes in practically quantitative yields.

The expansion of the traditional frames of the classical Staudinger reaction has resulted in the synthesis of numerous new compounds with nitrogen–phosphorus bonds. Even after nine decades, the reaction is still with a lot of unspent potential and it continues to intrigue and stimulate researchers.

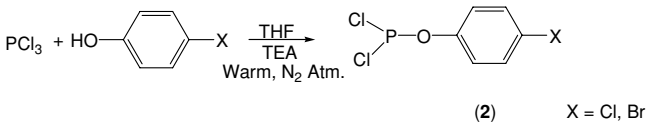
RESULTS AND DISCUSSION

Keeping the synthetic importance of the Staudinger reaction in view, *N*-[2-(4-halophenoxy)-3-(3-chlorophenyl)-3,4-dihydro-2*H*-1,3,2-λ^5-benzoxazaphosphinin-2-yliden]-N-substituted amines (**5–12**) were synthesized. The synthesis of the title compounds was accomplished in four steps.

By reacting salicylaldehyde with *m*-chloroaniline, in ethyl alcohol, Schiff's base was obtained. This Schiff's base was reduced by using $NaBH_4$/MeOH to afford the reduced Schiff's base (**1**).

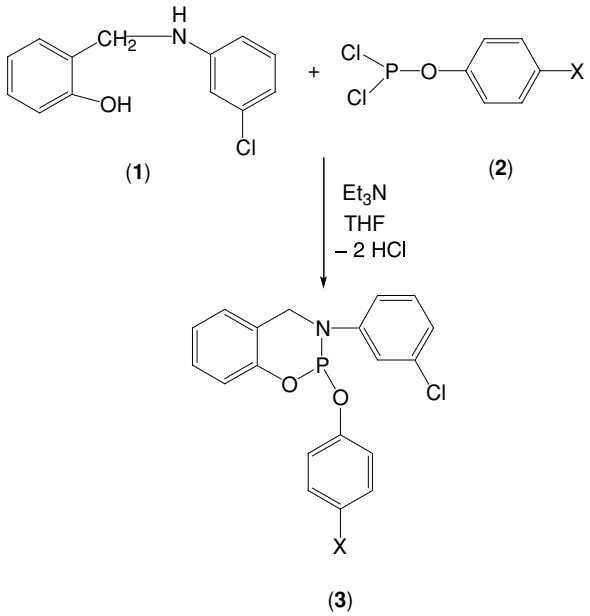


In the next step, *p*-chlorophenol/*p*-bromophenol was reacted with PCl_3 in THF in the presence of triethylamine under nitrogen atmosphere to get trivalent P(III) dichloride derivative (**2**).



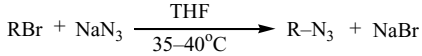
(**2**) X = Cl, Br

In the third step, **1** was reacted with **2** in equimolar quantities in the presence of Et_3N in THF to obtain the cyclized product **3**.



(**3**)

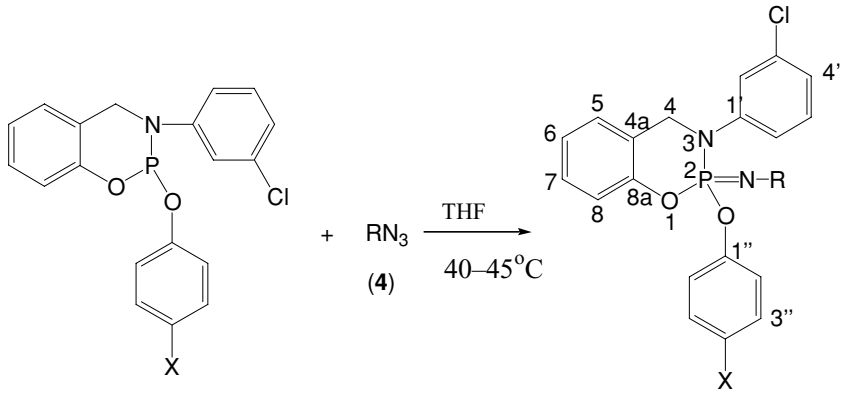
Alkyl azides were prepared by reacting alkyl bromides with sodium azide



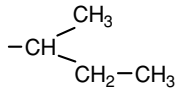
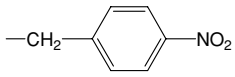
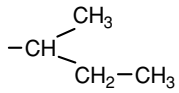
(**4**)

In the fourth step, **3** was reacted with various alkyl azides **4** to afford the title compounds **5–12** in optimum yields.

The synthetic and physical data of **5–12** are presented in Table 1. The infrared spectral study of all the title compounds (**5–12**) was made with a view to confirm the functional groups present in them. The infrared spectral data of the compounds **5–12** are presented in Table 1. All the compounds (**5–12**) exhibited characteristic absorption bands for P=N groups [10,11] in the region of 1219–1230 cm^{-1}. These compounds (**5–12**) exhibited characteristic infrared absorption bands in the region of 1345–1395 cm^{-1} for P—N stretching frequencies [10–12]. All the title compounds (**5–12**) showed characteristic absorption bands in the region of 1069–1093 cm^{-1} for $N—C_{(aliphatic)}$ stretching frequencies [10–12].



(**3**) (**5–12**)

Compound	R	X
5	– CH_2–CH_3	Cl
6		Cl
7	–CH_2–CH_2–CH_3	Cl
8		Cl
9	–CH_2 –CH=CH_2	Cl
10	–CH_2–CH_2–CH_2–CH_3	Cl
11	–CH_2–CH_3	Br
12		Br

SCHEME 1

The proton NMR chemical shifts of the compounds **5–12** are presented in Table 2. Aromatic protons of the title compounds (**5–12**) displayed a complex multiplet in the range of δ 6.07–8.20 [12]. The N—CH_2 protons of the heterocycle are resonated as a singlet in the region of δ 4.07–4.30.

Methylene protons of —CH_2—CH_3 in **5** are resonated as multiplet in the range of δ 1.43–1.62, and methyl protons are resonated as triplet at δ 0.92. Methylene protons of —CH_2—CH_2—CH_3 in **7** are resonated as multiplets in the range of δ 1.15–1.62, and its methyl protons are resonated as a triplet at δ 0.99. All other side chain protons are resonated in the expected regions.

The ^{13}C NMR spectral data of the compounds **5–12** are presented in Table 3. C-4 carbons in these compounds displayed signals in between δ 42.1 and 46.2. C-4a carbons resonated in the region of δ 129.0–130.7. C-8a carbons resonated in the region of δ 144.9–155.8. All other aromatic

TABLE 1 Synthesis, Physical, IR, and ^{31}NMR Data of *N*-[2-(4-Halophenoxy)-3-(3-chlorophenyl)-3,4-dihydro-2*H*-1,3,2-λ^5-benzoxaza phosphinin-2-yliden] *N*-Substituted Amines (**5–12**)

				Elemental Analysis Found (Calcd) (%)			*IR, ν (cm^{-1})*			
Compound	*mp (°C)*	*Yield (%)*	*Molecular Formula*	*C*	*H*	*N*	*P=N*	*P–N*	*N–C$_{(aliphatic)}$*	*^{31}P NMR δ (ppm)*
5	152–154	66	C_{21} H_{19} PN_2 O_2 Cl_2	58.26 (58.19)	4.43 (4.42)	6.56 (6.47)	1220	1385	1091	9.22
6	146–148	65	C_{23} H_{23} PN_2 O_2 Cl_2	59.94 (59.86)	4.96 (5.03)	6.11 (6.08)	1221	1395	1077	5.26
7	156–158	71	C_{22} H_{21} PN_2 O_2 Cl_2	59.13 (59.05)	4.68 (4.73)	6.25 (6.27)	1224	1371	1076	–3.56
8	147–148	68	C_{26} H_{20} PN_3 O_4 Cl_2	57.70 (57.77)	3.81 (3.73)	7.82 (7.78)	1226	1345	1093	–4.64
9	160–162	64	C_{22} H_{19} PN_2 O_2 Cl_2	59.41 (59.32)	4.31 (4.30)	6.39 (6.30)	1219	1376	1076	–4.67
10	150–152	67	C_{23} H_{23} PN_2 O_2 Cl_2	59.95 (59.86)	4.99 (5.03)	6.11 (6.08)	1220	1382	1076	9.18
11	144–146	67	C_{21} H_{19} PN_2 O_2 ClBr	52.78 (52.78)	4.06 (4.01)	5.88 (5.87)	1219	1360	1069	8.78
12	156–158	64	C_{23} H_{23} PN_2 O_2 ClBr	54.64 (54.60)	4.51 (4.59)	5.49 (5.54)	1230	1357	1074	8.44

carbons exhibited signals in the expected region. Ethyl, *n*-butyl, secondary butyl, and allylic carbons in the side chain showed signals in the expected regions.

^{31}P NMR data of all the compounds **5–12** are presented in Table 1. ^{31}P NMR chemical shifts of the title compounds appeared in the region of δ −4.66 to 9.22 [10,13]. Mass spectral data of **6–9** are presented in Table 4.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Mel-Temp apparatus and are uncorrected. IR spectra were recorded in KBr pellets on a Perkin–Elmer FT-IR 1000 spectrophotometer. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were taken on Bruker ACF NMR spectrophotometer operating at 400, 100, and 161.89 MHz, respectively, in $CDCl_3$ or DMSO-d_6 and were referenced to TMS (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Mass spectral data were collected on LCMS-2010 A Shimadzu spectrometer.

Synthesis of Allyl Azide

In a dry 100 mL round-bottomed flask fitted with a dropping funnel, calcium chloride guard tube, sodium azide (0.33 g, 0.005 mol) in 10 mL of dry THF was taken. Allyl bromide (0.61 g, 0.005 mol) in 40 mL of dry THF was added to sodium azide at room temperature with stirring. Later the reaction temperature was raised to 40–45°C and stirred for 4 h. The mixture was cooled to room temperature, and NaBr was filtered off. The filtrate containing allyl azide was used for the next step reaction without further purification.

*Synthesis of N-[2-(4-Chlorophenoxy)-3-(3-chlorophenyl- 3,4-dihydro-2H-1,3,2-λ^5-benzoxazaphosphinin-2-yliden]-N-allyl Amine (**9**)*

2-[(3-Chlorophenylamino)methyl] phenol (reduced Schiff's base) (1.17 g, 0.005 mol) in 30 mL of dry THF was added to 4-chlorophenylphosphorodichloridate (1.15 g, 0.005 mol) in 20 mL of dry THF in the presence of TEA under N_2 atmosphere at room temperature. After the addition, the reaction mixture was stirred for 4 h at 40–45°C. The progress of the reaction was judged by TLC analysis. The reaction mixture was filtered to remove triethlamine hydrochloride. To the filtrate, allylazide (0.005 mol) in 10 mL of THF was added at room temperature. The completion of the reaction was monitored by TLC analysis

TABLE 2 ^{1}H NMR Chemical Shifts of **5–12**

Compound	*Ar–H*	*N–CH_2*	*Hydrogens of R*
5	6.44–6.91 (m, 12H)	4.09 (s, 2H)	1.43–1.62 (m, 2H, –$\underline{CH_2}$–CH_3), 0.92 (t, 3H, $J = 11.6$ Hz, —CH_2–$\underline{CH_3}$)
6	6.17–6.97 (m, 12H)	4.07 (s, 2H)	1.62–1.86 [m, $\underline{CH}(CH_3)CH_2CH_3$], 0.98 [d, 3H, $J = 8.6$ Hz, $CH(\underline{CH_3})CH_2CH_3$], 1.24–1.37 [m, 2H, $CH(CH_3)\underline{CH_2}CH_3$], 0.89 [t, 3H, $J = 8.2$ Hz, $CH(CH_3)CH_2\underline{CH_3}$]
7	6.66–6.97 (m. 12H)	4.21 (s, 2H)	1.15–1.32 (m, 2H, –$\underline{CH_2}$—CH_2–CH_3), 1.47–1.62 (m, 2H, —CH_2–$\underline{CH_2}$—CH_3), 0.99 (t, 3H, $J = 6.8$ Hz, —CH_2—CH_2–$\underline{CH_3}$)
8	6.62–7.26 (m, 12H)	4.12 (s, 2H)	2.81 [s, 2H, $\underline{H_2}C\ C_6H_4$ *p*-(NO_2)], 7.47–8.2 [m, 4H, $\underline{H_2}C\ C_6H_4$ *p*-(NO_2), Ar–H].
9	6.66–7.77 (m, 12H)	4.27 (s, 2H)	1.86–2.89 (m, 2H , –$\underline{H_2}$C—CH=CH_2), 5.98–6.16 (m, 1H, —H_2C—$\underline{CH}$=CH_2), 5.25 (d, 2H, $J = 12$ Hz, —H_2C—CH=$C\underline{H_2}$)
10	6.08–7.05 (m, 12H)	4.21 (s, 2H)	1.12–1.27 (m, 2H, –$\underline{H_2}$C—CH_2—CH_2—CH_3), 1.31–1.38 (m, 2H, —H_2C–$\underline{CH_2}$ CH_2 CH_3), 1.41–1.56 (m, 2H, —H_2C—CH_2–$\underline{CH_2}$—CH_3), 0.88 (t, 3H, $J = 6.8$ Hz, —H_2C—CH_2—CH_2–$\underline{CH_3}$)
11	6.07–7.27 (m, 12H)	4.30 (s, 2H)	1.38–1.46 (m, 2H, –$\underline{CH_2}$—CH_3), 0.94 (t, 3H, $J = 9.6$ Hz, —H_2C–$\underline{CH_3}$)
12	6.64–7.17 (m, 12H)	4.27 (s, 2H)	1.68–1.88 [m, 1H, $\underline{CH}$ (CH_3) CH_2 CH_3], 1.12 [d, H, $J = 8.6$ Hz, CH $(\underline{CH_3})$ CH_2 CH_3], 1.26–1.42 [m, 2H, CH (CH_3) $\underline{CH_2}$ CH_3], 0.92 [t, 3H, $J = 8.2$ Hz, CH (CH_3) CH_2 $\underline{CH_3}$]

TABLE 3 ^{13}C NMR Data of **5–12**

Compound	*^{13}C NMR Data*
5	42.1 (C-4), 129.1 (C-5), 121. 1 (C-6), 128.9 (C-7), 115.6 (C-8), 129.0 (C-4a), 144.9 (C-8a), 144.9 (C-1′), 115.3 (C-2′), 134.4 (C-3′), 116.4 (C-4′), 129.7 (C-5′), 110.2 (C-6′), 147.1 (C-1″), 116.8 (C-2″ and C-6″),130.2 (C-3″ and C-5″), 127.0 (C-4″), 20.2 (–$\underline{H_2}$C—CH_3), 16.9 (—H_2C–$\underline{CH_3}$)
6	43.8 (C-4), 129.2 (C-5), 121.1 (C-6), 128.9 (C-7), 115.4 (C-8), 129.9 (C-4a), 147.2 (C-8a), 147.4 (C-1′), 115.5 (C-2′), 134.4 (C-3′), 116.9 (C-4′), 131.6 (C-5′), 111.7 (C-6′), 149.6 (C-1″), 116.9 (C-2″ and C -6″) , 130.8 (C-3″ and C-5″), 127.2 (C-4″), 30.8 [$\underline{CH}$ (CH_3) CH_2 CH_3], 24.1 [CH $(\underline{CH_3})$ CH_2 CH_3], 34.6 [CH (CH_3) $\underline{CH_2}$ CH_3], 8.1 [CH (CH_3) CH_2 $\underline{CH_3}$]
7	44.2 (C-4), 129.2 (C-5), 121.2 (C-6), 129.0 (C-7), 115.6 (C-8), 129.2 (C-4a), 145.6 (C-8a), 147.2 (C-1′), 115.0 (C-2′), 134.7 (C-3′), 116.4 ($\underline{C\text{-}4}$′), 130.2 (C-5′), 111.3 (C-6′), 148.9 (C-1″), 116.8 (C-2″ and C-6″), 129.5 (C-3″ and C-5″), 127.3 (C-4″), 46.0 (–$\underline{H_2}$C—CH_2—CH_3), 27.3 (—H_2C–$\underline{CH_2}$—CH_3), 10.2 (—H_2C—CH_2–$\underline{CH_3}$)
8	43.8 (C-4), 129.2 (C-5), 122.1 (C-6), 128.7 (C-7), 115.9 (C-8), 130.7 (C-4a), 147.2 (C-8a), 145.4 (C-1′), 113.5 (C-2′), 135.2 (C-3′), 117.8 (C-4′), 131.3 (C-5′), 116.5 (C-6′), 150.2 (C-1″), 117.8 (C-2″ and C-6″), 130.3 (C-3″ and C-5″), 117.4 (C-4″), 38.2 ($\underline{CH_2}$—Ar—NO_2), 145.2 (C-1‴), 128.7 (C-2‴ and C-6‴), 122.4 (C-3‴ and C-5‴), 147.2 (C-4‴)
9	46.0 (C-4), 129.4 (C-5), 121.6 (C-6), 129.0 (C-7), 115. 6 (C-8), 129.9 (C-4a), 155.8 (C-8a), 134.9 (C-1′), 114.1 (C-2′), 134.7 (C-3′), 117.0 (C-4′), 130.7 (C-5′), 116.0 (C-6′), 31.4 (–$\underline{H_2}$C—CH=CH_2), 130.3 (—H_2C–$\underline{HC}$=CH_2), 116.8 (—H_2C—CH=C$\underline{H_2}$), 155.7 (C-1″), 117.3 (C-2″ and C-6 ″), 134.9 (C-3″ and C-5 ″), 117.0 (C-4 ″)
10	42.1 (C-4), 129.9 (C-5), 122.2 (C-6), 129.1 (C-7), 116.8 (C-8), 130.3 (C-4a), 155.0 (C-8a), 147.3 (C-1), 113.8 (C-2′), 134.8 (C-3′), 117.6 (C-4′) 130.4 (C-5′), 117.2 (C-6′), 150.0 (C-1″), 119.7 (C-2″ and C-6″), 129.9 (C-3″ and C-5″) 117.7 (C-4″), 43.2 (–$\underline{H_2}$C—CH_2—CH_2—CH_3), 35.1 (—H_2C–$\underline{CH_2}$—CH_2—CH_3), 20.5 (—H_2C—CH_2–$\underline{CH_2}$—CH_3),13.2 (—H_2C—CH_2—CH_2–$\underline{CH_3}$)
11	42.3 (C-4), 129.9 (C-5), 129.4 (C-6), 121.2 (C-7), 115.8 (C-8), 130.2 (C-4a), 155.5 (C-8a), 148.5 (C-1′), 114.2 (C-2′), 134.6 (C-3′), 117.3 (C-4′), 131.9 (C-5′), 111.1 (C-6′), 150.6 (C-1″), 117.3 (C-2″ and 6″), 130.2 (C-3″ and C-5″), 127.1 (C-4″), 27.3 (–$\underline{CH_2}$—CH_3), 20.3 (—CH_2–$\underline{CH_3}$)
12	46.2 (C-4), 129.3 (C-5), 129.0 (C-6), 120.8 (C-7), 115.9 (C-8), 130.3 (C-4a), 155.7 (C-8a), 153.7 (C-1′), 114.3 (C-2′), 135.0 (C-3′), 117.5 (C-4′), 132.0 (C-5′), 112.0 (C-6′), 154.5 (C-1″), 117.5 (C-2″ and C-6″), 130.3 (C-3″ and 5″), 129.4 (C-4″), 35.7 [$\underline{CH}$ (CH_3) CH_2 CH_3], 23.1 [CH $(\underline{CH_3})$ CH_2 CH_3], 32.7 [CH (CH_3) $\underline{CH_2}$ CH_3], 8.5 [CH (CH_3) CH_2 $\underline{CH_3}$]

(hexane–ethyl acetate, 3:1). The solvent was removed in a rota-evaporator. The crude iminophosphorane **(9)** thus obtained was further purified by column chromatography using silica gel (60–120 mesh) as adsorbent and hexane and ethyl acetate (2:1) as an eluent to afford analytically pure iminophosphorane **(9)** as a solid. Other members of the series were prepared by adopting the above procedure.

TABLE 4 Mass Spectral Data of **6–9**

Compound	*m/z(%)*
6	462 [13, $(M + 1)^+$], 461 (100, $M^{+\bullet}$), 460 [24, $(M - 1)^+$], 381 (37)
7	448 [36, $(M + 1)^+$], 447 (100, $M^{+\bullet}$), 446 [14, $(M - 1)^+$], 405 (9)
8	541 [24, $(M + 1)^+$], 540 (100, $M^{+\bullet}$), 478 (15), 454 (6)
9	446 [50, $(M + 1)^+$], 445 (100, $M^{+\bullet}$), 431(20), 341(12), 233(30)

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