ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 2, pp. 324–326. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © A.A. Prishchenko, M.V. Livantsov, O.P. Novikova, L.I. Livantsova, E.R. Milaeva, 2008, published in Zhurnal Obshchei Khimii, 2008, Vol. 78, No. 2, pp. 339–341.

LETTERS TO THE EDITOR

Acylation of Aryl-substituted Bis(aminomethyl)phosphinic Acids

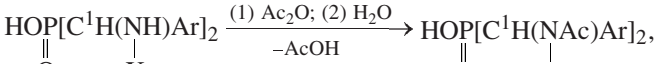
A. A. Prishchenko, M. V. Livantsov, O. P. Novikova, L. I. Livantsova, and E. R. Milaeva

Lomonosov Moscow State University, Vorob'evy Gory, Moscow, 119992 Russia
e-mail: liv@org.chem.msu.su

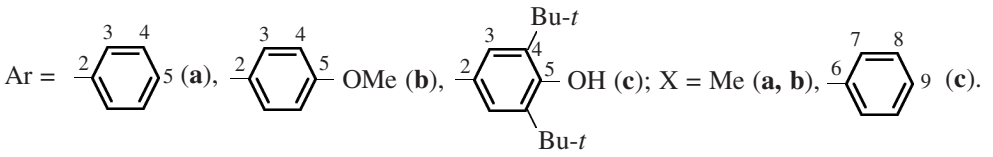
Received May 18, 2007

DOI: 10.1134/S1070363208020278

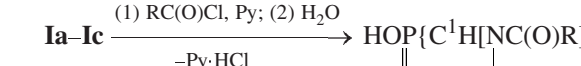
Phosphorus-substituted carboxamides of various structure are widely used in organic synthesis and present certain interest as effective ligands and biologically active compounds [1]. In the present work we propose convenient methods for preparing a number of phosphorus-substituted amides of acetic and oleic [(*Z*)-octadec-9-enoic] acids on the basis of recently synthesized arylsubstituted bis(aminomethyl)phosphinic acids [2]. Phosphorus-substituted acetamides **II** were prepared in high yields by heating a mixture of amine **I** with excess acetic anhydride followed by treatment of the reaction mixture with water and recrystallization of the product aqueous ethanol.



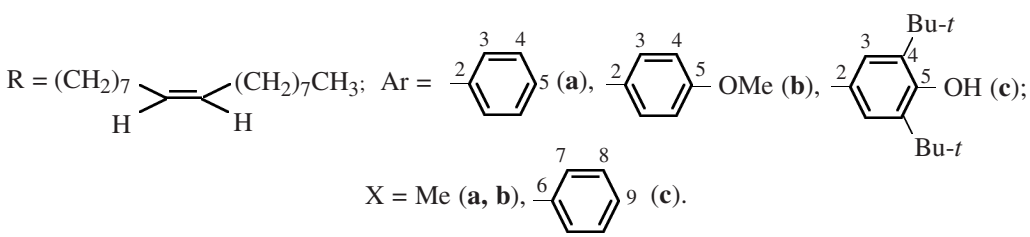
Ia–Ic **IIa–IIc**



The reaction of amines **I** with excess oleoyl chloride in the presence of pyridine under the same conditions gave phosphorus-substituted oleamides **III** in high yield.



IIIa–IIIc



Bis-amines **Ia** and **Ib** we described earlier [2] but bis-amine **Ic** was specially prepared by an analogous method. The synthesized compounds **Ic**–**III** are promising ligands and biologically active substances, for example, antioxidants, and phosphorus-substituted oleamides **III** can also be applied as micelle-forming agents.

The NMR spectra of compounds **Ic**–**III** show, together with characteristic signals of the PC^1HN fragments, signals of aromatic and acetyl or oleoyl fragments (vide infra). According to the NMR spectra, compounds **Ic**–**III** are mixtures of two stereoisomers whose ratio was determined from the ^{31}P NMR spectra (data for the prevailing isomer are given first). Because of the low contents of the second isomer in phosphinate **IIb**, we present for it ^{31}P NMR data only (cf. [3]).

Bis[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(*N*-phenylamino)methyl]phosphinic acid (Ic) was prepared as described in [2], yield 87%, mp 181°C. First isomer (65%), ^1H NMR spectrum, δ_H, ppm: 1.28 s (Me_3C), 4.44 d (C^1H, $^2J_{PH}$ 16 Hz), 7.19 s (C^3H), 6.3–7.0 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 30.91 s (*Me*$_3$C), 34.96 s (Me_3C), 55.13 d (C^1, $^1J_{PC}$ 101 Hz), 127.73 s (C^2), 124.99 s (C^3), 138.91 s (C^4), 153.24 s (C^5), 148.38 d (C^6, $^3J_{PC}$ 13 Hz), 113.96 s (C^7), 128.99 s (C^8), 116.90 s (C^9). ^{31}P NMR spectrum, δ_P, ppm: 40.06 s. Second isomer. ^1H NMR spectrum, δ_H, ppm: 1.32 s (Me_3C), 4.77 d (C^1H, $^2J_{PH}$ 16 Hz), 7.13 s (C^3H), 6.3–7.0 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 30.80 s (*Me*$_3$C), 34.87 s (Me_3C), 55.28 d (C^1, $^1J_{PC}$ 98 Hz), 127.73 s (C^2), 125.24 s (C^3), 139.00 s (C^4), 153.38 s (C^5), 148.16 d (C^6, $^3J_{PC}$ 12 Hz), 113.83 s (C^7), 129.56 s (C^8), 117.36 s (C^9). ^{31}P NMR spectrum, δ_P, ppm: 39.65 s. Found, %: C 73.52; H 8.26. $C_{42}H_{57}N_2O_4P$. Calculated, %: C 73.66; H 8.39.

Bis[(*N*-acetyl-*N*-methylamino)(phenyl)methyl]-phosphinic acid (IIa). A mixture of 3.1 g of amine **Ia**, 15 ml of acetic anhydride, and 20 ml of methylene chloride was heated under reflux with stirring for 2 h, after which 20 ml of water was added, and the mixture was heated to boil. The solvents were then removed in a vacuum. Water, 20 ml, 5 ml of ethanol, and 5 ml of ether were added to the residue, and the mixture was stirred for 0.5 h. Ether was separated, and the crystals were filtered off, washed with ether, and exposed to a vacuum of 1 mm Hg for 1 h to obtain 3.2 g (82%) of compound **IIa**, mp 96°C. First isomer (69%), ^1H NMR spectrum, δ_H, ppm: 6.03 d (C^1H, $^2J_{PH}$ 16 Hz), 3.07 s (MeN), 7.0–7.6 m (C_6H_5), 1.99 s (Ac). ^{13}C NMR spectrum, δ_C, ppm: 54.51 d (C^1, $^1J_{PC}$ 98 Hz), 130.06 d (C^2, $^2J_{PC}$ 5 Hz), 128.0–129.0 m (C^3, C^4, C^5), 170.86 d (C=O, $^3J_{PC}$ 5 Hz), 33.80 s (MeN), 22.03 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 37.12 s. Second isomer, ^1H NMR spectrum, δ_H, ppm: 5.04 d (C^1H, $^2J_{PH}$ 16 Hz), 2.98 s (MeN), 7.0–7.6 m (C_6H_5), 1.80 s (Ac). ^{13}C NMR spectrum, δ_C, ppm: 54.28 d (C^1, $^1J_{PC}$ 100 Hz), 129.96 d (C^2, $^2J_{PC}$ 4 Hz), 128.0–129.0 m (C^3, C^4, C^5), 171.13 d (C=O, $^3J_{PC}$ 4 Hz), 33.32 s (MeN), 21.70 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 35.88 s. Found, %: C 61.68; H 6.52. $C_{20}H_{25}N_2O_4P$. Calculated, %: C 61.85; H 6.49.

Compounds **IIb** and **IIc** were synthesized by the same procedure.

Bis[(4-methoxyphenyl)(*N*-methyl-*N*-acetylamino)methyl]phosphinic acid (IIb). Yield 86%, mp 89°C. First isomer (75%), ^1H NMR spectrum, δ_H, ppm: 5.96 d (C^1H, $^2J_{PH}$ 16 Hz), 6.88 d (C^3H, $^3J_{HH}$ 8 Hz), 7.43 d (C^4H, $^3J_{HH}$ 8 Hz), 3.06 s (MeN), 3.74 s (MeO), 2.00 s (Ac). ^{13}C NMR spectrum, δ_C, ppm: 53.60 d (C^1, $^1J_{PC}$ 100 Hz), 131.39 d (C^2, $^2J_{PC}$ 7 Hz), 131.58 d (C^3, $^3J_{PC}$ 6 Hz), 114.16 s (C^4), 159.17 s (C^5), 170.63 d (C=O, $^3J_{PC}$ 4 Hz), 33.53 s (MeN), 55.47 s (MeO), 22.04 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 37.70 s. Second isomer. ^1H NMR spectrum, δ_H, ppm: 6.02 d (C^1H, $^2J_{PH}$ 16 Hz), 6.91 d (C^3H, $^3J_{HH}$ 8 Hz), 7.50 d (C^4H, $^3J_{HH}$ 8 Hz), 2.98 s (MeN), 3.70 s (MeO), 1.91 s (Ac). ^{13}C NMR spectrum, δ_C, ppm: 53.40 d (C^1, $^1J_{PC}$ 100 Hz), 130.79 d (C^2, $^2J_{PC}$ 8 Hz), 131.92 d (C^3, $^3J_{PC}$ 6 Hz), 114.31 s (C^4), 158.95 s (C^5), 170.77 d (C=O, $^3J_{PC}$ 4 Hz), 33.27 s (MeN), 55.47 s (MeO), 21.55 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 36.26 s. Found, %: C 58.72; H 6.59. $C_{22}H_{29}N_2O_6P$. Calculated, %: C 58.92; H 6.52.

Bis[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(*N*-phenyl-*N*-acetylamino)methyl]phosphinic acid (IIc). Yield 74%, mp 139°C. First isomer (97%), ^1H NMR spectrum, δ_H, ppm: 6.35 d (C^1H, $^2J_{PH}$ 16 Hz), 6.7–7.7 m (C_6H_2, C_6H_5), 2.03 s (Ac), 1.24 s (2*t*-Bu). ^{13}C NMR spectrum, δ_C, ppm: 58.12 d (C^1, $^1J_{PC}$ 104 Hz), 127–139 m (C_6H_2, C_6H_5), 153.94 s (C^5), 119.43 s (C^7), 123.35 s (C^9), 169.19 s (C=O), 34.69 s (Me_3C), 30.60 s (*Me*$_3$C), 23.68 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 34.65 s. Second isomer. ^{31}P NMR spectrum, δ_P, ppm: 34.35 s. Found, %: C 71.64; H 8.07. $C_{46}H_{61}N_2O_6P$. Calculated, %: C 71.85; H 8.00.

Bis[(*N*-methyl-*N*-oleoylamino)(phenyl)methyl]-phosphinic acid (IIIa). To a cooled (10°C) and stirred mixture of 3.1 g of amine **Ia**, 5 ml of pyridine, and 30 ml of methylene chloride, 7.7 g of oleoyl chloride in 10 ml of methylene chloride was added. The mixture was heated for 3 h and leaft to stand for

12 h. The precipitate was filtered off. The filtrate was diluted with 20 ml and heated for 1 h. The solvents were then removed in a vacuum. Water, 20 ml, 10 ml of hexane, and 3 ml of ether were added to the residue, and the mixture was stirred for 0.5 h. Hexane was separated and water was distilled off in a vacuum of 1 mm Hg for 1 h to obtain 4.9 g (78%) of compound **IIIa** as an oil. First isomer (73%), ^{1}H NMR spectrum, δ_H, ppm: 6.23 d (C^1H, $^2J_{PH}$ 16 Hz), 7.0-7.6 m (C_6H_5), 5.25–5.40 m (CH=CH), 3.12 s (MeN), 1.3–2.0 m ($14CH_2$), 0.90 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 54.38 d (C^1, $^1J_{PC}$ 98 Hz), 128.0–131.0 m (C_6H_5, CH=CH), 172.56 s (C=O), 33.66 s (MeN), 22–32 m ($14CH_2$), 13.59 s (MeC). ^{31}P NMR spectrum, δ_P, ppm: 35.95 s. Second isomer. ^{1}H NMR spectrum, δ_H, ppm: 6.31 d (C^1H, $^2J_{PH}$ 16 Hz), 7.0–7.6 m (C_6H_5), 5.25–5.40 m (CH=CH), 3.07 s (MeN), 1.3–2.0 m ($14CH_2$), 0.90 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 53.94 d (C^1, $^1J_{PC}$ 103 Hz), 126.0–131.0 m (C_6H_5, CH=CH), 172.72 s (C=O), 33.66 s (MeN), 22–32 m ($14CH_2$), 13.59 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 33.38 s. Found, %: C 70.65; H 8.94. $C_{36}H_{55}N_2O_4P$. Calculated, %: C 70.79; H 9.07.

Compounds **IIIb** and **IIIc** were prepared by the same method.

Bis[(4-methoxyphenyl)(*N*-methyl-*N*-oleoylamino)methyl]phosphinic acid (IIIb). Yield 80%, oil. First isomer (60%), ^{1}H NMR spectrum, δ_H, ppm: 6.06 d (C^1H, $^2J_{PH}$ 16 Hz), 6.70 d (C^3H, $^3J_{HH}$ 8 Hz), 7.45 d (C^4H, $^3J_{HH}$ 8 Hz), 5.2–5.3 m (CH=CH), 3.06 s (MeN), 3.65 s (MeO), 1.2–2.0 m ($14CH_2$), 0.82 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 53.94 d (C^1, $^1J_{PC}$ 100 Hz), 127–132 m (C^2, C^3, CH=CH), 113.68 s (C^4), 159.00 s (C^5), 173.10 s (C=O), 34.21 s (MeN), 55.00 s (MeO), 22–31 m ($14CH_2$), 14.09 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 36.25 s. Second isomer. ^{1}H NMR spectrum, δ_H, ppm: 6.13 d (C^1H, $^2J_{PH}$ 16 Hz), 6.77 d (C^3H, $^3J_{HH}$ 8 Hz), 7.53 d (C^4H, $^3J_{HH}$ 8 Hz), 5.2–5.3 m (CH=CH), 3.01 s (MeN), 3.68 s (MeO), 1.2–2.0 m ($14CH_2$), 0.82 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 54.05 d (C^1, $^1J_{PC}$ 99 Hz), 127–132 m (C^2, C^3, CH=CH), 113.97 s (C^4), 159.35 s (C^5), 173.55 s (C=O), 34.79 s (MeN), 55.00 s (MeO), 22–31 m ($14CH_2$), 14.09 s (*Me*C). ^{31}P NMR spectrum, δ_P, ppm: 33.55 s. Found, %: C 67.82; H 8.74. $C_{38}H_{59}N_2O_6P$. Calculated, %: C 68.03; H 8.86.

Bis[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(*N*-phenyl-*N*-oleoylamino)methyl]phosphinic acid (IIIc). Yield 72%, oil. First isomer (65%), ^{1}H NMR spectrum, δ_H, ppm: 5.98 d (C^1H, $^2J_{PH}$ 16 Hz), 6.8–7.6 m (C_6H_2, C_6H_5), 5.2–5.3 m (CH=CH), 1.1–2.0 m ($14CH_2$, 2*t*-Bu), 0.78 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 60.29 d (C^1, $^1J_{PC}$ 102 Hz), 127–139 m (C_6H_2, C_6H_5, CH=CH), 153.83 s (C^5), 119.49 s (C^7), 122.86 s (C^9), 174.69 s (C=O), 34.04 s (Me_3C), 22–32 m ($14CH_2$, $2Me_3C$), 14.08 s (Me_3C). ^{31}P NMR spectrum, δ_P, ppm: 35.11 s. Second isomer. ^{1}H NMR spectrum, δ_H, ppm: 6.09 d (C^1H, $^2J_{PH}$ 16 Hz), 6.8–7.6 m (C_6H_2, C_6H_5), 5.2–5.3 m (CH=CH), 1.1–2.0 m ($14CH_2$, 2*t*-Bu), 0.78 t (*Me*CH_2, $^3J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 60.40 d (C^1, $^1J_{PC}$ 100 Hz), 127–139 m (C_6H_2, C_6H_5, CH=CH), 153.58 s (C^5), 119.49 s (C^7), 122.86 s (C^9), 174.11 s (C=O), 34.15 s (Me_3C), 22–32 m ($14CH_2$, $2Me_3C$), 14.08 s (*Me*CH_2). ^{31}P NMR spectrum, δ_P, ppm: 36.77 s. Found, %: C 74.89; H 9.03. $C_{62}H_{91}N_2O_6P$. Calculated, %: C 75.12; H 9.25.

The NMR spectra were recorded on a Bruker Avance 400 spectrometer in $(CD_3)_2SO$ against TMS (^{1}H, ^{13}C) or 85% solution of H_3PO_4 in D_2O (^{31}P).

ACKNOWLEDGMENTS

The work was financially supported by the Russian Foundation for Basic Research (project no. 05-03-32 864).

REFERENCES

1. Petrov, K.A., Chauzov, V.A., and Erokhina, T.S., *Usp. Khim.,* 1974, vol. 43, no. 11, p. 2045; Kukhar', V.P. and Solodenko, V.A., *Usp. Khim.,* 1987, vol. 56, no. 9, p. 1504; Kolodyazhnyi, O.I., *Usp. Khim.,* 2006, vol. 75, no. 3, p. 254.
2. Prishchenko, A.A., Livantsov, M.V., Novikova, O.P., and Livantsova L.I., *Zh. Obshch. Khim.,* 2007, vol. 77, no. 9, p. 1574.
3. Prishchenko, A.A., Livantsov, M.V., Kustrya, D.N., Novikova, O.P., Grigor'ev, E.V., and Goncharova, Zh.Yu., *Zh. Obshch. Khim.,* 1997, vol. 67, no. 11, p. 1914; Prishchenko, A.A., Novikova, O.P., Livantsov, M.V., Kustrya, D.N., and Grigor'ev, E.V., *Zh. Obshch. Khim.,* 1998, vol. 68, no. 3, p. 514.