ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 12, pp. 1576–1577. © Pleiades Publishing, Ltd., 2012.
Original Russian Text © V.V. Andriyashin, Yu.V. Bakhtiyarova, R.A. Cherkasov, V.I. Galkin, I.V. Galkina, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 12, pp. 1605–1606.

SHORT COMMUNICATIONS

Synthesis of Quaternary Phosphonium Salts on the Basis of 2,6-Di-*tert*-butyl-4-methylphenol

V. V. Andriyashin, Yu. V. Bakhtiyarova, R. A. Cherkasov, V. I. Galkin, and I. V. Galkina

Kazan (Volga Region) Federal University, ul. Kremlevskaya 18, Kazan, 420008 Tatarstan, Russia
e-mail: vig54@mail.ru

Received May 21, 2012

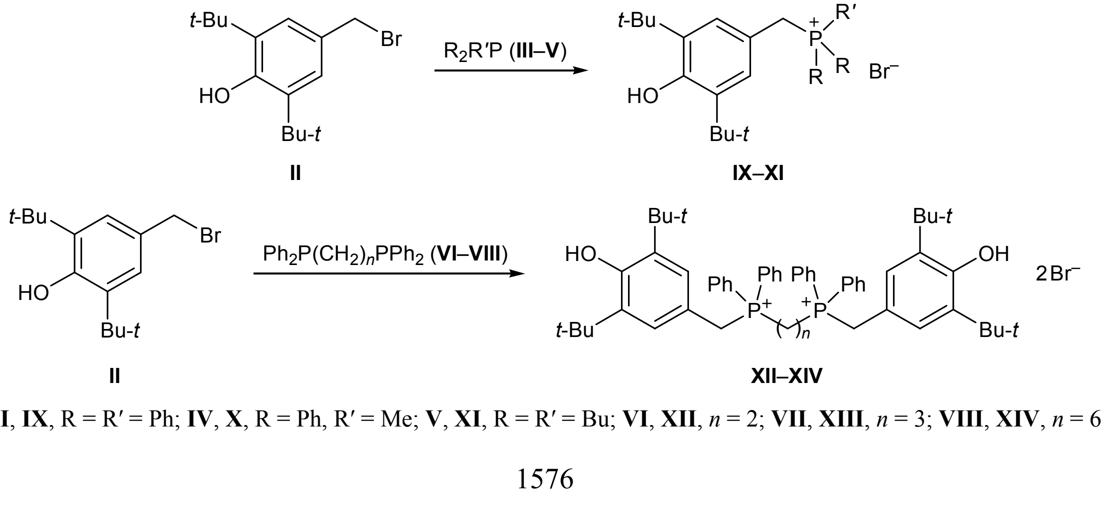
DOI: 10.1134/S1070428012120160

Phosphorus-containing 2,6-di-*tert*-butyl-4-methylphenol derivatives exhibit a broad spectrum of antibacterial and antimycotic activity and are widely used as antioxidants [1, 2]. Depending on the substituents on the phosphorus atom, these compounds are active against pathogenic microorganisms in humans and animals, in particular against *Staphylococcus aureus, Escherichia coli, Salmonella paratyphi B*, *Pseudomonas aeruginosa*, and *Candida albicans*. We previously described a procedure for the synthesis of quaternary phosphonium derivatives of 2,6-di-*tert*-butyl-4-methylphenol (**I**) by quaternization of tertiary phosphines with 3,5-di-*tert*-butyl-4-hydroxybenzyl bromide (**II**) which was prepared by bromination of phenol **I** with *N*-bromosuccinimide [3]. The reactions of benzyl bromide **II** with triphenylphosphine (**III**), methyldiphenylphosphine (**IV**), and tributylphosphine (**V**), as well as with 1,2-bis(diphenylphosphino)ethane (**VI**), 1,3-bis(diphenylphosphino)propane (**VII**), and 1,6-bis(diphenylphosphino)hexane (**VIII**), in diethyl ether at room temperature gave the corresponding crystalline phosphonium salts **IX**–**XIV**.

The ^{31}P NMR spectra of **IX**–**XIV** contained only one signal in the region δ_P 23.2–33.4 ppm, which corresponds to the phosphonium group. In the ^{1}H NMR spectra of these compounds, a singlet at δ 2.5 ppm from protons in the *tert*-butyl groups, a doublet at δ ~6 ppm from the methylene protons, a singlet at δ 7 ppm from the OH proton, and a doublet at δ 8.0–8.5 ppm from protons in the *meta* positions of the phenol ring were observed. The structure of phosphonium salt **XII** was confirmed by X-ray analysis; the results will be reported elsewhere. All newly synthesized phosphonium salts showed a high antimicrobial activity.

4-Bromomethyl-2,6-di-*tert*-butylphenol (II) was synthesized as described in [3]. mp 56°C. ^{1}H NMR spectrum (CH$_3$OD), δ, ppm: 2.80 s [18H, C(CH$_3$)$_3$], 5.97 s (1H, CH$_2$Br), 7.00 s (1H, OH), 8.62 s (2H, C$_6$H$_2$). Found, %: C 60.54; H 8.01. $C_{15}H_{23}BrO_4$. Calculated, %: C 60.21; H 7.75.

Phosphonium salts IX–XIV (*general procedure*). Equimolar amounts (0.001 mol) of bromide **II** in 5 ml



III, **IX**, R = R′ = Ph; **IV**, **X**, R = Ph, R′ = Me; **V**, **XI**, R = R′ = Bu; **VI**, **XII**, *n* = 2; **VII**, **XIII**, *n* = 3; **VIII**, **XIV**, *n* = 6.

of diethyl ether and the corresponding tertiary phosphine or bis-phosphine in 5 ml of diethyl ether were mixed together at room temperature, and the mixture was kept for 10–20 min. The precipitate was filtered off and washed with diethyl ether.

(3,5-Di-*tert*-butyl-4-hydroxybenzyl)triphenylphosphonium bromide (IX). Yield 0.533 g (95%), mp 225°C (decomp.). ^{1}H NMR spectrum (CH_3OD), δ, ppm: 2.58 s [18H, $C(CH_3)_3$], 5.92 d (2H, CH_2, J_{PH} = 13.87 Hz), 7.00 s (1H, OH), 8.09 d (2H, C_6H_2, J_{PH} = 2.69 Hz), 8.87–9.28 m (15H, C_6H_5). ^{31}P NMR spectrum (CH_3OD): δ_P 23.4 ppm. Found, %: C 70.70; H 7.00; P 5.62. $C_{33}H_{38}BrOP$. Calculated, %: C 70.58; H 6.82; P 5.52.

(3,5-Di-*tert*-butyl-4-hydroxybenzyl)methyl(diphenyl)phosphonium bromide (X). Yield 0.489 g (98%), mp 242°C (decomp.). ^{1}H NMR spectrum (CH_3OD), δ, ppm: 2.65 s [18H, $C(CH_3)_3$], 3.70 d (3H, CH_3, J_{PH} = 13.68 Hz), 5.63 d (2H, CH_2, J_{PH} = 14.41 Hz), 7.02 s (1H, OH), 8.17 d (2H, C_6H_2, J_{PH} = 2.78 Hz), 9.04–9.25 m (10H, C_6H_5). ^{31}P NMR spectrum (CH_3OD): δ_P 23.2 ppm. Found, %: C 67.40; H 7.29; P 6.17 $C_{28}H_{36}BrOP$. Calculated, %: C 67.33; H 7.26; P 6.20.

Tributyl(3,5-di-*tert*-butyl-4-hydroxybenzyl)phosphonium bromide (XI). Yield 0.476 g (95%), colorless crystals, mp 188°C (decomp.). ^{1}H NMR spectrum (CH_3OD), δ, ppm: 2.27–3.47 m (27H, C_4H_9), 2.80 s [18H, $C(CH_3)_3$], 4.90 d (2H, CH_2, J_{PH} = 14.09 Hz), 7.11 s (1H, OH), 8.45 d (2H, C_6H_2, J_{PH} = 2.52 Hz). ^{31}P NMR spectrum (CH_3OD): δ_P 33.4 ppm. Found, %: C 64.82; H 10.19; P 6.17. $C_{27}H_{50}BrOP$. Calculated, %: C 64.66; H 10.05; P 6.18.

Ethane-1,2-diylbis[(3,5-di-*tert*-butyl-4-hydroxybenzyl)diphenylphosphonium] dibromide (XII). Yield 0.463 g (93%), mp 195°C (decomp.). ^{31}P NMR spectrum (CH_3OD): δ_P 29.2 ppm. Found, %: C 67.53; H 7.14; P 6.20. $C_{56}H_{70}Br_2O_2P_2$. Calculated, %: C 67.47; H 7.08; P 6.21.

Propane-1,3-diylbis[(3,5-di-*tert*-butyl-4-hydroxybenzyl)diphenylphosphonium] dibromide (XIII). Yield 0.454 g (90%), mp 215°C (decomp.). ^{31}P NMR spectrum (CH_3OD): δ_P 24.9 ppm. Found, %: C 67.74; H 7.25; P 6.20. $C_{57}H_{72}Br_2O_2P_2$. Calculated, %: C 67.72; H 7.18; P 6.13.

Hexane-1,6-diylbis[(3,5-di-*tert*-butyl-4-hydroxybenzyl)diphenylphosphonium] dibromide (XIV). Yield 0.481 (92%), mp 162°C (decomp.). ^{31}P NMR spectrum (C_2D_5OD): δ_P 25.4 ppm. Found, %: C 68.65; H 7.51; P 5.94. $C_{60}H_{78}Br_2O_2P_2$. Calculated, %: C 68.44; H 7.47; P 5.88.

The ^{1}H and ^{31}P NMR spectra were recorded on a Bruker Avance-400 spectrometer; the chemical shifts were determined relative to the residual proton signal of the solvent (^{1}H) or 85% H_3PO_4 (^{31}P, external reference).

REFERENCES

1. Zenkov, N.K., Kandalintseva, N.V., Lankin, V.Z., Menytsikova, E.B., and Prosenko, A.E., *Fenol'nye bioantioksidanty* (Phenolic Bioantioxidants). Novosibirsk: Sib. Otd. Ross. Akad. Med. Nauk, 2003.
2. Ovchinnikova, L.P., Rotskaya, U.N., Vasyunina, E.A., Sinitsina, O.I., Kandalintseva, N.V., Prosenko, A.E., and Nevinskii, G.A., *Bioorg. Khim.*, 2009, vol. 35, p. 417.
3. Kim, D.H. and Kummerow, F.A., *J. Am. Chem. Soc.*, 1961, vol. 39, p. 150.