ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 11, pp. 1703–1705. © Pleiades Publishing, Ltd., 2007.
Original Russian Text © N.G. Khusainova, E.A. Berdnikov, O.A. Mostovaya, S.M. Rybakov, R.A. Cherkasov, 2007, published in Zhurnal Organicheskoi Khimii, 2007, Vol. 43, No. 11, pp. 1703–1705.

Reactions of Allenyl- and Vinylphosphonates with Imidazole

N. G. Khusainova, E. A. Berdnikov, O. A. Mostovaya, S. M. Rybakov, and R. A. Cherkasov

Butlerov Chemical Institute, Kazan State University, ul. Kremlevskaya 18, Kazan, 420008 Tatarstan, Russia
e-mail: narkis.khusainova@ksu.ru

Received January 4, 2007

Abstract—Dialkyl 3-methylbuta-1,2-dienyl- and vinylphosphonates take up imidazole at the β-carbon atom in the unsaturated fragment to give the corresponding β-(1*H*-imidazol-1-yl)alkenyl- and alkylphosphonates.

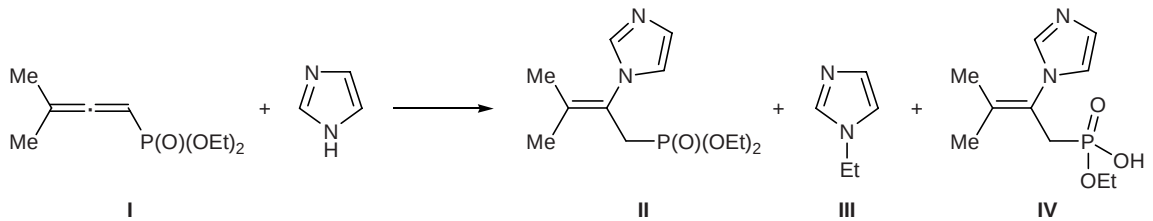
DOI: 10.1134/S107042800711019X

Derivatives of alkenyl- and alkylphosphonic acids having nitrogen-containing groups in the β-position attract interest as potential biologically active compounds with a broad spectrum of action, complexing agents, and extractants [1–4]. The simplest and convenient method for the synthesis of β-aminophosphonates is based on reaction of unsaturated four-coordinate phosphorus acid derivatives with primary and secondary amines [5–7]. However, methods of synthesis and properties of alkenyl- and alkylphosphonates having nitrogen-containing heterocyclic substituents in the β-position have been studied insufficiently [1]. The present article reports on the results of our study on the reactions of dialkyl allenyl- and vinylphosphonates with imidazole with a view to obtain new potential biologically active derivatives.

The ^{31}P NMR spectrum of the reaction mixture obtained from diethyl 3-methylbuta-1,2-dien-1-ylphosphonate (**I**) and imidazole contained two phosphorus signals at δ_P 26.2 and 25.4 ppm with an intensity ratio of 10:1. Distillation of the mixture gave compound **II** which showed only one signal at δ_P 26 ppm in the ^{31}P NMR spectrum. In the ^{1}H NMR spectrum of adduct **II** we observed a doublet at δ 2.86 ppm ($^2J_{PH}$ = 21.3 Hz), which is typical of methylene protons in the α-position with respect to phosphorus, and doublet signals from two methyl groups attached to a double-bonded carbon atom. These findings suggest that imidazole adds at the 1,2-double bond of cumulene **I** to give diethyl 2-(1*H*-imidazol-1-yl)-3-methylbut-2-en-1-ylphosphonate (**II**) (Scheme 1). Protons in the imidazole ring of compound **II** give rise to three broadened signals at δ 6.88, 7.00, and 7.40 ppm in the ^{1}H NMR spectrum, in keeping with published data for N-substituted imidazole derivatives [8].

Apart from signals belonging to adduct **II**, the ^{1}H NMR spectrum of the reaction mixture contained the following weak signals, δ, ppm: 1.27 m (3H, $^3J_{HH}$ = 7, $^5J_{HH}$ = 1 Hz), 4.00 m (2H), 6.96 br.s (1H), 7.02 br.s (1H), 7.06 br.s (1H); these signals were assigned to *N*-ethylimidazole (**III**). Presumably, the reaction is accompanied by partial dealkylation of the phosphonate fragment of compound **I** or **II** with formation of acidic ester **IV** and *N*-ethylimidazole (**III**). The formation of ethyl hydrogen phosphonate **IV** is confirmed by the presence in the ^{1}H NMR spectrum of a methylene proton signal at 3.01 ppm with a coupling constant $^2J_{PH}$ of 20.9 Hz; in addition, several triplets from methyl protons in the ethoxy groups of **II** and **IV** are overlapped in the δ region 1.2–1.3 ppm. Protons of the OCH_2 groups in structures **II** and **IV** appear as overlapped multiplets at δ 4.00 ppm. Compound **IV** is

Scheme 1.



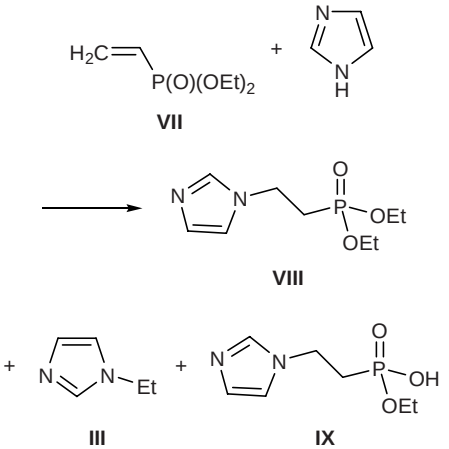
I **II** **III** **IV**

likely to be characterized by a high boiling point, so that it cannot be isolated by distillation. The ability of unsaturated methyl and ethyl phosphonates to undergo dealkylation of the ester moiety was noted by us previously [9, 10].

Likewise, the reaction of imidazole with diisopropyl 3-methylbuta-1,2-dien-1-ylphosphonate (**V**) afforded diisopropyl 2-(1*H*-imidazol-1-yl)-3-methylbut-2-en-1-ylphosphonate (**VI**) via addition of the heterocycle at the central carbon atom of the cumulated bond system. As followed from the ^{1}H and ^{31}P NMR spectra of the reaction mixture, the process is not accompanied by dealkylation of the phosphonate fragment. On the other hand, the addition of imidazole to allene activated by an ethoxycarbonyl group, catalyzed by stoichiometric amount of triphenylphosphine, occurred at the terminal carbon atom of the cumulene system [8].

According to the ^{1}H and ^{31}P NMR data, diethyl vinylphosphonate (**VII**) reacted with imidazole to give β-imidazolylethylphosphonate **VIII**, ethyl hydrogen phosphonate **IX**, and ethylimidazole **III** (Scheme 2). The ^{31}P NMR spectrum of the reaction mixture contained two signals at δ_P 27.2 and 26.9 ppm at a ratio of 1:0.1. The signal at δ_P 26.9 ppm was assigned to the phosphorus nucleus in ethyl hydrogen 2-(1*H*-imidazol-1-yl)ethylphosphonate (**IX**). The formation of **IX** is also confirmed by the presence in the ^{1}H NMR spectrum of the reaction mixture of overlapping multiplets at δ 2 and 4 ppm from the PCH_2 and OCH_2 protons in **VIII** and **IX**. Methyl protons in the ethoxy group of acidic ester **IX** resonate as a triplet at δ 1.31 ppm ($^3J_{HH}$ = 7.1 Hz). Distillation of the reaction mixture gave compound **VIII** which displayed only one signal at δ_P 27 ppm in the ^{31}P NMR spectrum.

Scheme 2.



In the reaction of dibutyl vinylphosphonate (**X**) with imidazole we obtained dibutyl 2-(1*H*-imidazol-1-yl)ethylphosphonate (**XI**) as the only product.

Thus nucleophilic addition of imidazole to allenyl- and vinylphosphonates occurs at the β-carbon atom of the unsaturated fragment to give the corresponding β-imidazolylalkenyl- and -alkylphosphonates.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer. The ^{1}H and ^{31}P NMR spectra were obtained on a Varian Unity-300 instrument at 300 MHz for ^{1}H and 121.42 MHz for ^{31}P from solutions in $CDCl_3$. The chemical shifts were measured relative to the residual solvent signal (^{1}H; $CHCl_3$, δ 7.24 ppm) or 85% phosphoric acid (^{31}P, external reference).

Reaction of imidazole with dialkyl allenylphosphonates (*general procedure***).** A mixture of 1 mmol of phosphonate **I** or **V** and 1 mmol of imidazole was heated at 85–90°C until the cumulene absorption band at 1955 cm^{-1} (νC=C=C) disappeared from the IR spectrum of the mixture. The products were isolated by distillation under reduced pressure.

Diethyl 2-(1*H*-imidazol-1-yl)-3-methylbut-2-en-1-ylphosphonate (II). Yield 1.23 g (33%), mp 36°C, bp 123°C (0.04 mm). ^{1}H NMR spectrum, δ, ppm: 1.18 t (6H, C**H**$_3$CH$_2$O, $^3J_{HH}$ = 7.3 Hz), 1.46 d (3H, =CCH$_3$, $^5J_{PH}$ = 6.1 Hz), 1.84 d (3H, =CCH$_3$, $^5J_{PH}$ = 4.9 Hz), 2.86 d (2H, CH_2P, $^2J_{PH}$ = 21.3 Hz), 3.92 m (4H, CH_2O), 6.88 d.d (1H, 4-H, $^3J_{HH}$ = 1.2, $^4J_{HH}$ = 0.9 Hz), 7.00 d.d (1H, 5-H, $^3J_{HH}$ = 1.2, $^4J_{HH}$ = 0.9 Hz), 7.40 d.d (1H, 2-H, $^4J_{HH}$ = 0.9, $^4J_{HH}$ = 0.9 Hz). ^{31}P NMR spectrum: δ_P 26 ppm. Found, %: C 52.58; H 7.9; P 10.89. $C_{12}H_{21}N_2O_3P$. Calculated, %: C 52.93; H 7.77; P 11.32.

Diisopropyl 2-(1*H*-imidazol-1-yl)-3-methylbut-2-en-1-ylphosphonate (VI). Yield 2.2 g (72%), bp 122–124°C (0.03 mm), n_D^{20} = 1.4858. ^{1}H NMR spectrum, δ, ppm: 1.00 d [6H, (C**H**$_3$)$_2$CHO, $^3J_{HH}$ = 6.2 Hz], 1.06 d [6H, (C**H**$_3$)$_2$CHO, $^3J_{HH}$ = 6.2 Hz], 1.31 d (3H, CH_3C=, $^5J_{PH}$ = 6.0 Hz), 1.70 d (3H, CH_3C=, $^5J_{PH}$ = 4.6 Hz), 2.68 d (2H, CH_2P, $^2J_{PH}$ = 21.2 Hz), 4.44 d.sept (2H, CHOP, $^3J_{HH}$ = 6.2, $^3J_{PH}$ = 7.6 Hz), 6.75 d.d (1H, 4-H, $^3J_{HH}$ = 1.3, $^4J_{HH}$ = 1.1 Hz), 6.84 d.d (1H, 5-H, $^3J_{HH}$ = 1.3, $^4J_{HH}$ = 0.9 Hz), 6.95 d.d (1H, 2-H, $^4J_{HH}$ = 1.1, $^4J_{HH}$ = 0.9 Hz). ^{31}P NMR spectrum: δ_P 22.7 ppm. Found, %: C 56.32; H 8.18; P 9.91. $C_{14}H_{25}N_2O_3P$. Calculated, %: C 56.01; H 8.33; P 10.32.

Reaction of imidazole with vinylphosphonates (*general procedure*). A mixture of 1 mmol of vinylphosphonate **VII** or **X** and 1 mmol of imidazole was heated for 20–22 h at 85–90°C and was then distilled under reduced pressure.

Diethyl 2-(1*H*-imidazol-1-yl)ethylphosphonate (VIII). Yield 0.55 g (28%), bp 131–132°C (0.05 mm), n_D^{20} = 1.4834. ^{1}H NMR spectrum, δ, ppm: 1.21 t (6H, C**H**$_3$CH$_2$O, $^3J_{HH}$ = 7.0 Hz), 2.14 m (2H, CH$_2$P, $^2J_{PH}$ = 18.9 Hz), 3.97 m (4H, CH$_2$OP), 4.14 m (2H, NCH$_2$, $^3J_{PH}$ = 12.2 Hz), 6.86 br.s (1H, 4-H), 6.96 br.s (1H, 5-H), 7.42 br.s (1H, 2-H). ^{31}P NMR spectrum: δ_P 27 ppm. Found, %: C 42.01; H 7.18; P 12.91. $C_9H_{17}N_2O_3P$. Calculated, %: C 42.24; H 7.33; P 13.36.

Dibutyl 2-(1*H*-imidazol-1-yl)ethylphosphonate (XI). Yield 1.3 g (43%), bp 145–147°C (0.07 mm), n_D^{20} = 1.4749. ^{1}H NMR spectrum, δ, ppm: 0.93 t (6H, C**H**$_3$CH$_2$, $^3J_{HH}$ = 7.3 Hz), 1.37 m (4H, CH$_2$), 1.62 m (4H, CH$_2$), 2.42 m (2H, CH$_2$P, $^2J_{PH}$ = 18.7 Hz), 4.01 m (4H, CH$_2$OP), 4.22 m (2H, NCH$_2$, $^3J_{PH}$ = 11.6 Hz), 6.94 d.d (1H, 4-H, $^3J_{HH}$ = 1.2, $^4J_{HH}$ = 1.0 Hz), 7.05 d.d (1H, 5-H, $^3J_{HH}$ = 1.2, $^4J_{HH}$ = 1.0 Hz), 7.50 d.d (1H, 2-H, $^4J_{HH}$ = 1.0, 1.0 Hz). ^{31}P NMR spectrum: δ_P 26.5 ppm. Found, %: C 54.62; H 8.28. $C_{13}H_{25}N_2O_3P$. Calculated, %: C 54.16; H 8.68.

REFERENCES

1. *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity*, Kukhar, V.P. and Hudson, H.R., New York: Wiley, 2000.
2. Palacios, F., Alonso, C., and de los Santos, J.M., *Chem. Rev*., 2005, vol. 105, p. 899.
3. Kafarski, P. and Lejczak, B., *Curr. Med. Chem. Anti-Cancer Agents*, 2001, vol. 1, p. 301.
4. Cherkasov, R.A., Galkin, V.I., Khusainova, N.G., Mostovaya, O.A., Garifzyanov, A.R., Nuriazdanova, G.Kh., Krasnova, N.S., and Berdnikov, E.A., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1481.
5. Pudovik, A.N. and Denisova, G.M., *Zh. Obshch. Khim*., 1953, vol. 23, p. 263.
6. Khusainova, N.G., Mostovaya, O.A., Berdnikov, E.A., Litvinov, I.A., Krivolapov, D.B., and Cherkasov, R.A., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1260.
7. Panarina, A.E., Dogadina, A.V., Zakharov, V.I., and Ionin, B.I., *Tetrahedron Lett*., 2001, vol. 42, p. 4365.
8. Virieux, D., Guillouzic, A.-F., and Cristau, H.-J., *Tetrahedron*, 2006, vol. 62, p. 3710.
9. Pudovik, A.N. and Khusainova, N.G., *Zh. Obshch. Khim*., *Khimiya organicheskikh soedinenii phosphora* (Chemistry of Organic Phosphorus Compounds), 1967, p. 53.
10. Khusainova, N.G., Mostovaya, O.A., Nizamov, I.S., and Cherkasov, R.A., *Russ. J. Org. Chem*., 2004, vol. 40, p. 581.