

SHORT
COMMUNICATIONS

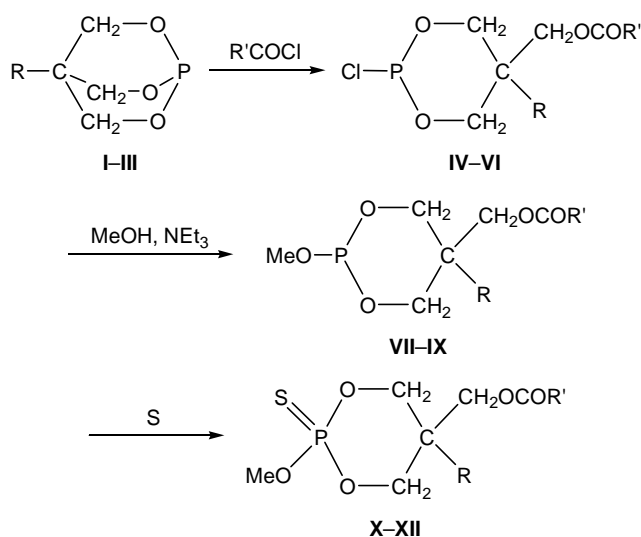
4-Alkyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octanes in the Synthesis of Lipids

G. A. Savin and O. M. Kutsemako

Volgograd State Pedagogical University, pr. Lenina 27, Volgograd, 400131 Russia

Received January 12, 2004

Proceeding with the previously initiated studies on the synthesis of nonglycerol polyol phospholipids [1, 2], the present communication reports on new phosphatide acid analogs on the basis of 4-alkyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octanes. In the first stage, readily accessible bicyclic phosphites **I–III** were brought into reaction with palmitoyl chloride. The acylation of **I–III** occurred at the oxygen rather than phosphorus atom [3] to afford phosphorochloridites **IV–VI**. The reactions were carried out without a solvent, by heating equimolar amounts of initial compound **I–III** and palmitoyl chloride in a sealed ampule for 36 h at 130–140°C. The formation of products **IV–VI** was monitored by ^{31}P NMR spectra which contained singlets at δ_{P} 148–149 ppm. Methanolysis of **IV–VI** in anhydrous diethyl ether in the presence of triethylamine on cooling to -10°C gave phosphites



**I, IV, VII, X, R = C₃H₇; II, V, VIII, XI, R = C₄H₉;
III, VI, IX, XII, R = C₅H₁₁; R' = C₁₅H₃₁.**

VII–IX. Compounds **VII–IX** (δ_{P} 125 ppm; R_{f} 0.6 [hexane–dioxane, 3:1 (A)], Silufol UV-254) were treated (without isolation from the reaction mixture) with elemental sulfur to obtain thiophosphates **X–XII**. This process took 2 h on heating in dry boiling benzene. Thiophosphates **X–XII** were purified by column chromatography on silica gel using benzene as eluent. Compounds **X–XII** showed a signal at δ_{P} 64 ppm in the ^{31}P NMR spectra.

Compound **X**. mp 45–46°C, R_{f} 0.5 [hexane–dioxane, 5:1 (B)]. Found, %: C 60.05; H 9.87; P 6.46. $\text{C}_{24}\text{H}_{47}\text{O}_5\text{PS}$. Calculated, %: C 60.22; H 9.90; P 6.47.

Compound **XI**. mp 48–50°C, R_{f} 0.5 (B). Found, %: C 60.82; H 10.00; P 6.27. $\text{C}_{25}\text{H}_{49}\text{O}_5\text{PS}$. Calculated, %: C 60.94; H 10.02; P 6.29.

Compound **XII**. mp 51–53°C, R_{f} 0.5 (B). Found, %: C 61.46; H 10.09; P 6.09. $\text{C}_{26}\text{H}_{51}\text{O}_5\text{PS}$. Calculated, %: C 61.63; H 10.14; P 6.11.

The ^1H NMR spectra of solutions of **X–XII** in CDCl_3 ($c = 0.5$ M) were recorded on a Bruker WM-250 spectrometer (250 MHz). The proton signals were assigned using the double resonance technique. The $^{31}\text{P}\text{--}\{^1\text{H}\}$ NMR spectra ($c = 1$ M) were obtained on a Bruker WP-80SY spectrometer (32.4 MHz) using 85% H_3PO_4 as external reference.

REFERENCES

- Savin, G.A., Kamneva, E.A., and Nifant'ev, E.E., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1048.
- Nifant'ev, E.E., Predvoditelev, D.A., and Savin, G.A., *Dokl. Akad. Nauk SSSR*, 1991, vol. 320, p. 905.
- Martynov, I.V., Fetisov, V.I., and Sokolov, V.B., *Itogi Nauki Tekhn., Ser. Org. Khim.*, 1989, no. 11, p. 3.