Heteroatom Chemistry
Volume 19, Number 4, 2008

# Novel Bile Acid Derived *H*-Phosphonate Conjugates: Synthesis and Spectroscopic Characterization

Yan Li, Weijun Chu, and Yong Ju

*Key Laboratory of Bio-organic Phosphorus Chemistry & Chemical Biology, Ministry of Education, Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China*

*Received 9 October 2007; revised 25 December 2007, 27 February 2008*

ABSTRACT: *The H-phosphonate bioconjugates of bile acids, conjugated with various alcohols and nucleosides, were obtained in one pot by a tandem transesterification with diphenyl phosphite (DPP). The synthesis of cholic acid derived phosphoramide from the corresponding H-phosphonate was also demonstrated. The structures of these novel conjugates were confirmed on the basis of IR,* $^{31}P$ *NMR,* $^{1}H$ *NMR, and mass spectra. The synthesized bile acid conjugates were mixtures of diastereoisomers due to the chirality of the phosphorus.* © 2008 Wiley Periodicals, Inc. Heteroatom Chem 19:402–407, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20447

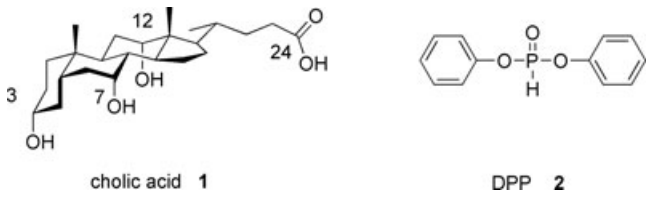
## *INTRODUCTION*

Bile acid is a class of biogenetic compounds and plays a prominent role in biological systems [1]. The medicinal properties of bile acids and their conjugates have been discussed in the literature with promising results [2–4]. Besides their biological importance, the rigid concave of the hydrophobic backbone and the unique disposition of hydroxyl groups make these compounds attracting building blocks for the construction of environmentally responsive amphiphiles [5] and functional supramolecular systems [6].

It is especially true for the case of cholic acid **1**, which is one of the primary bile acids found in human and a rare naturally occurring molecule exhibiting facial amphiphilicity [5]. It possesses one carboxylic acid and three hydroxyl groups, which render various chemical modifications possible. However, one of the major problems associated with the synthesis of cholic acid conjugates is that these "natural" hydroxyl groups are relatively inert, especially the 7α- and 12α-OH [6]. A number of articles have reported the conversion of the hydroxyls to other functional groups. For instance, Davis et al. have used 11 high yielding steps to replace three hydroxyls by amine groups [7]. The "triamino-analogue" of methyl cholate is explored as a precursor to design anion receptors and a scaffold for combinatorial chemistry [8]. Savage and his coworkers have reported cholic acid derived anionic facial amphiphiles with three carboxyl groups, which can aggregate at very low concentration [9]. To develop new cross-linking reagents in polymeric gels, Zhu's group has prepared cholic acid derivatives with multiple methacrylate groups by the use of methacrylic acid, methacryloyl chloride, and methacryloyl anhydride as acylating agents [10].

*H*-Phosphonate has been proven to be a versatile building block in organic synthesis. It can be further transferred to phosphate, phosphorothioate, and phosphoroselenoate by oxidation [11]

*Correspondence to:* Yong Ju; e-mail: juyong@tsinghua.edu.cn.
Contract grant sponsor: National Science Foundation of China.
Contract grant number: 20772071.
Contract grant sponsor: Specialized Research Fund for the Doctoral Program of Higher Education.
Contract grant number: 20050003104.



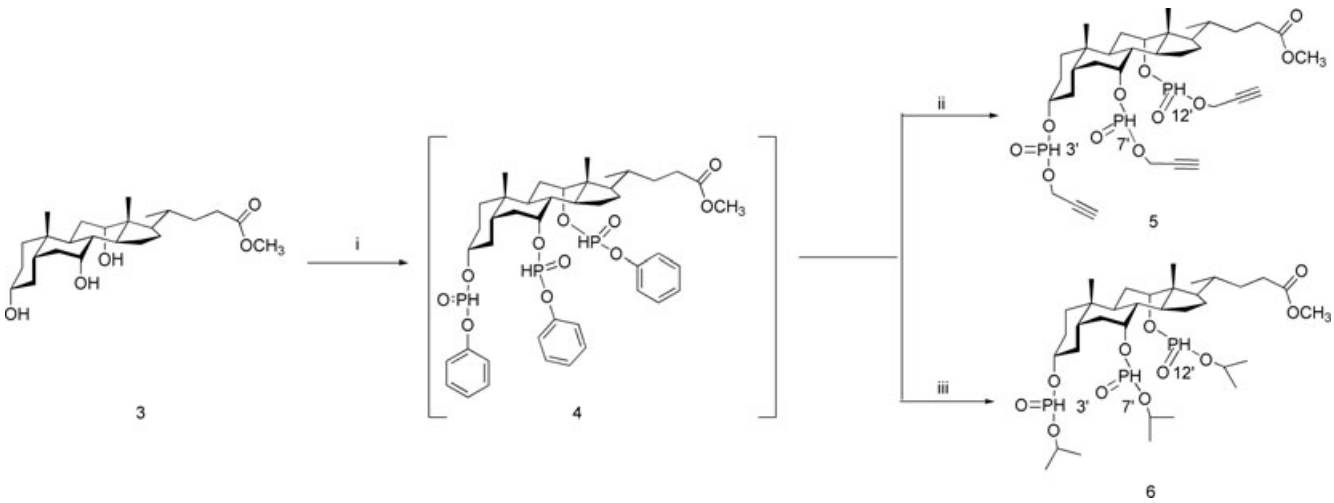

**SCHEME 1** Chemical structure of cholic acid and diphenyl phosphite.

as well as phosphoramidate by the Atherton–Todd reaction in high yield [12]. In addition, phosphate derivatives are important intermediates in biological metabolism [13] and are widely used in pharmaceutical industry [14]. Diphenyl phosphite (DPP, **2**; see Scheme 1), which can undergo fast transesterification with various alcohols in pyridine, is used as an effective phosphorylation reagent in the synthetic process [15]. To obtain mono-phenyl *H*-phosphonates, a large excess of DPP (7 equiv.) was required to prevent the formation of double-exchange *H*-phosphonates [16]. However, our previous work showed that if one of the hydroxyl components is sterically hindered moiety, the desired mono-phenyl *H*-phosphonate can be obtained in high yield [17]. The hydroxyls on the bile acids are oriented along one face and are typical steric hindered groups. Taking account of these facts, bile acids are ideal starting structures to prepare multifunctional scaffolds containing phosphorus. In this paper, we report the synthesis and characterization of *H*-phosphonates derived bile acid conjugates.

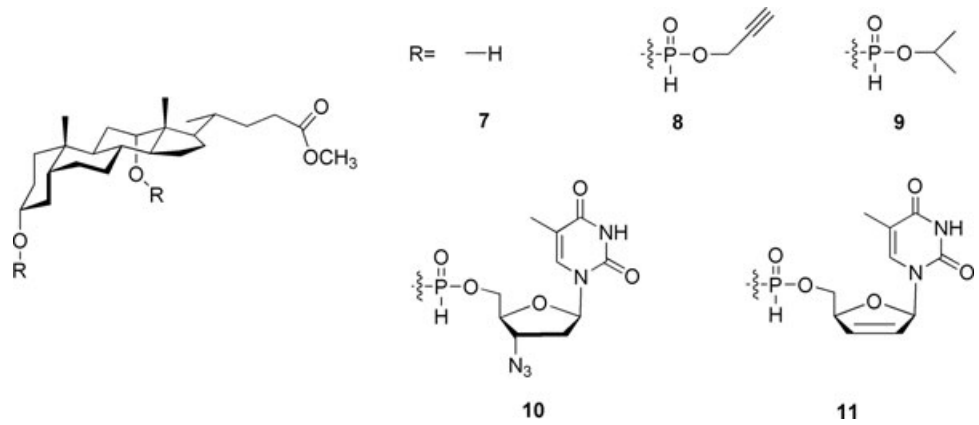
## *RESULTS AND DISCUSSION*

The general synthetic strategy for bile acid *H*-phosphonates conjugates is shown in Schemes 2 and 3. Our approach starts from methyl cholate because it can be prepared easily in large quantities and has much better solubility in pyridine than cholic acid. Many other bile acid derived esters and amides are also appropriate starting materials. The reaction was monitored by ESI-MS and $^{31}$P NMR. The first step of transesterification is fast, and all hydroxyl groups were converted to mono-phenyl *H*-phosphonates **4** in 5 h under anhydrous condition, evidenced by the peak of ion $[M + Na]^+$ at 866 $m/z$ on the ESI-MS spectrometry. However, this intermediate is very unstable and could not to be isolated. The second step transesterification between the mono-phenyl phosphonates and the corresponding alcohol is relatively slow and is sensitive to steric hindrance, thereby effectively preventing the formation of di-steroid *H*-phosphonate.

The deoxycholic acid derived *H*-phosphonate conjugates were also synthesized in a similar procedure. It is worth mentioning that some bioactive nucleosides, such as 3′-azido-3′-deoxythymidine (AZT) and 2′,3′-didehydro-2′,3′-dideoxythymidine (D4T), possess one primary alcohol group. These nucleosides can also be attached to the deoxycholic acid methyl ester using similar tandem transesterification with DPP. Bile acids are interesting carriers that target a specific organ and improve the lipophilicity for drug molecules [2]. These compounds containing both steroid and nucleosides have the potential to act as prodrugs or drugs by themselves. However,




**SCHEME 2** Synthesis and chemical structure of H-phosphonate derivatives of cholic acid. (i) DPP, py, 0°C, 5 h; (ii) propargyl alcohol, py, 8 h; (iii) *i*-PrOH, py, 8 h.

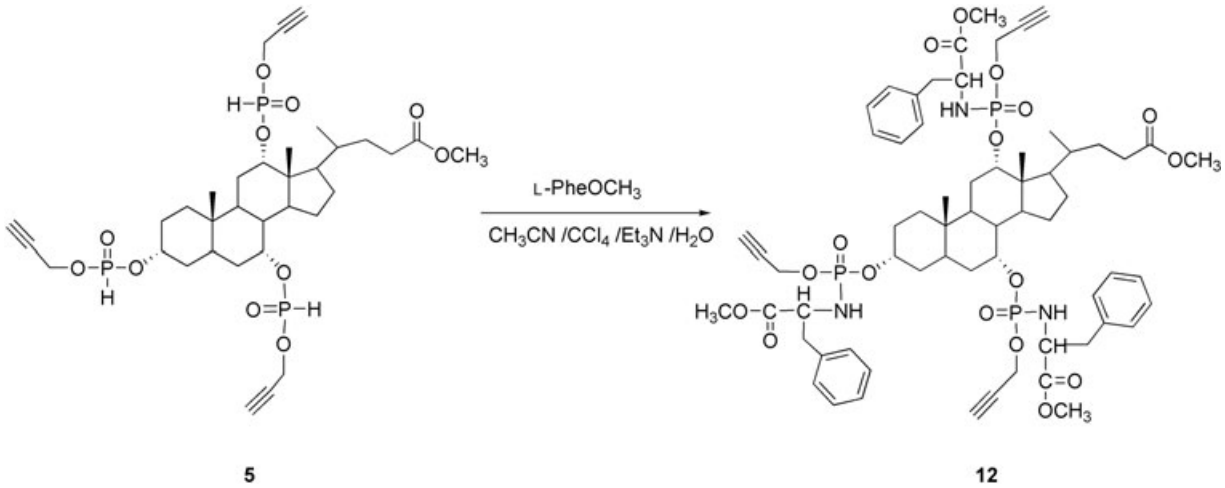



**SCHEME 3** Chemical structure of H-phosphonate derivatives of deoxycholic acid.

three relatively large nucleoside moieties cannot be attached to the steroid nucleus simultaneously due to the steric hindrance. When the same reaction condition was applied to cholic acid methyl ester, only a complex mixture was obtained and could not be purified by chromatography on a silica gel.

Furthermore, the related bile acid derivatives could be easily obtained from the corresponding *H*-phosphonate. The synthesis of phosphoramidate with three molecules of L-phenylalanine methyl ester was demonstrated as an example, as shown in Scheme 4. Despite the large steric hindrance, the reaction proceeded well using the improved Atherton–Todd method [12]. The end of the reaction can be easily detected by the observation of the disappearance of the $^{1}J$ coupling constant (710 Hz) in the $^{31}$P NMR spectrum (coupled mode). The resulting phosphoramidate is tolerant to moisture and is much more stable than the corresponding *H*-phosphonates.

The structures of these newly synthesized *H*-phosphonate and phosphoramidate bile acid conjugates have been well confirmed by IR, $^{31}$P NMR, $^{1}$H NMR, and HRMS. Because the phosphorus in every *H*-phosphonate group is chiral and can readily change configuration between R and S, one bile acid *H*-phosphonates conjugate was in fact the mixture of several diastereoisomers [17,18]. Considering the fact that the corresponding carbons on the steroid nucleus (3-C, 7-C, and 12-C) are also chiral atoms, the splitting caused by the presence of diastereoisomers can be observed in both $^{31}$P and $^{1}$H NMR spectra. Figure 1 presents the characteristic resonance peaks in the cholic acid derivatives. From the NMR spectra, it was found that the 3-H, 7-H, and 12-H moved toward the lower field after




**SCHEME 4** Synthesis and chemical structure of cholic acid derived phosphoramide conjugate.

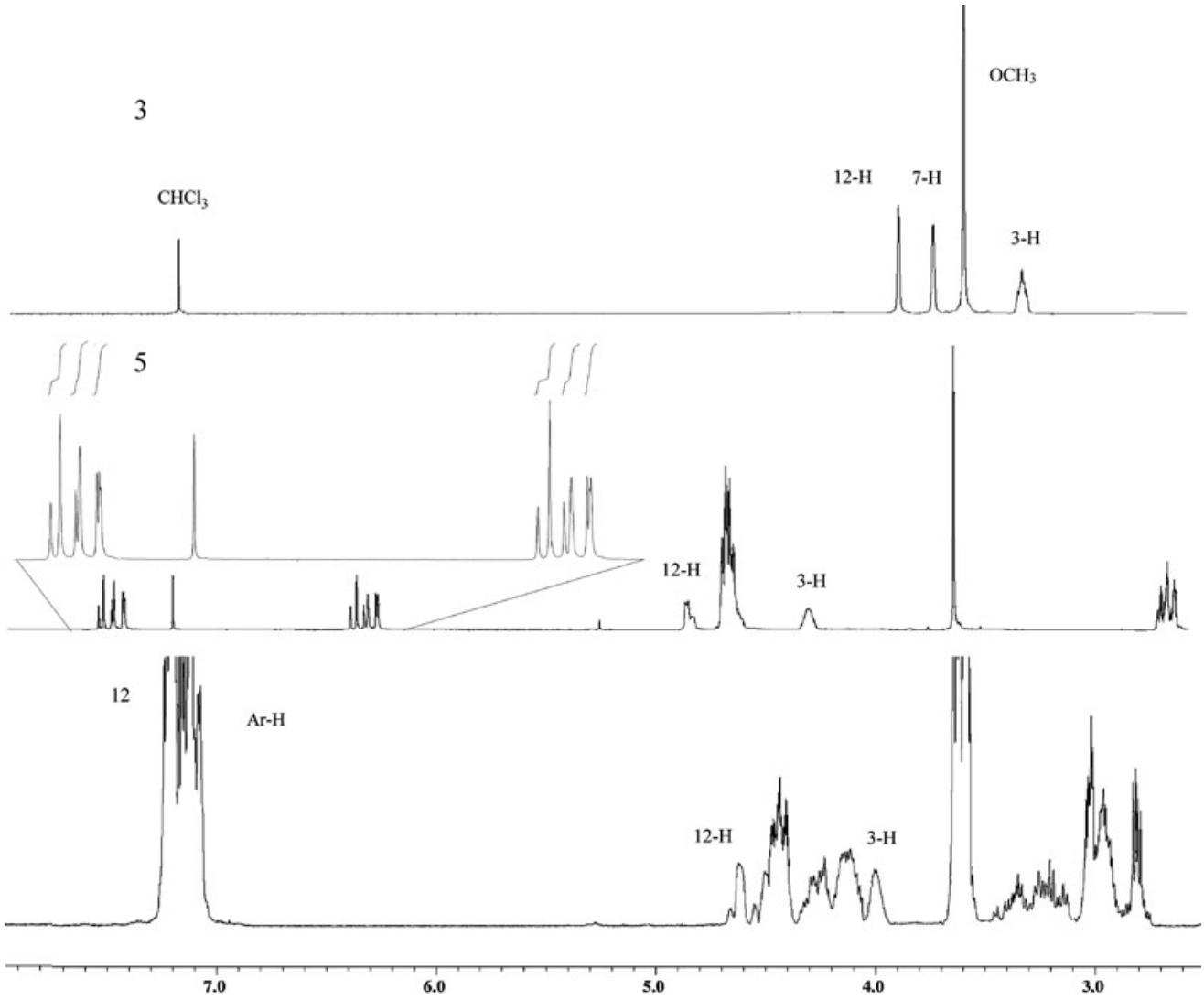



**FIGURE 1** Comparison of the 600 MHz 1H NMR spectra of compounds **3, 5**, and **12** in $CDCl_3$. The insert shows the detailed resonance peaks of **5** in the downfield. The signal of 7-H in compounds **5** and **12** was overlapped with propargyl protons according to 1H-1H COSY spectra.

phosphorylation. However, a slight reverse shift was observed when *H*-phosphonate was transferred into the phosphoramide group. In addition, the sharp peaks of 12-H and 7-H in the steroid nucleus were replaced by broader peaks in the *H*-phosphonate conjugate **5** and in the phosphoramidate conjugate **12**, indicating the presence of diastereoisomers.

The protons directly connected with phosphorus are easily identified by the $^1J_{P-H}$ coupling constant (about 700 Hz) in the downfield of $^1$H NMR spectrum. In 600 MHz NMR spectrum, resonance peaks of the three protons show two main groups due to the large $^1J_{P-H}$ coupling. It is interesting to note that each of the two groups can be divided into three small groups with same integral area, indicating that the distinguishable chemical shift of the three protons connected with phosphorus. Every small group was further splitted into two peaks, also suggesting the existence of diastereoisomers.

In conclusion, bile acids, which possess up to three steric hindered hydroxyl groups, have provided a unique structure for the synthesis of *H*-phosphonate derivatives. The above protocols for the preparation of *H*-phosphonate and phosphoramidate conjugates involve mild and efficient chemical transformations, which make multiple modifications at the steroid nucleus possible. According to NMR studies, the protons directly connected with phosphorus show distinguishable signals and the resulting products were a mixture of several diastereoisomers. To the best of our knowledge, this is the first report about direct phosphorylation on

the hydroxyl groups of bile acids. On the basis of the preliminary results, the extension of this methodology may find applications in pharmacology and supramolecular chemistry.

## EXPERIMENTAL

$^1$H NMR spectra were recorded at 300 MHz or 600 MHz for protons on JOEL JNM-ECA300 or JNM-ECA600 spectrometer. Chemical shifts ($\delta$) are given in ppm relative to TMS ($\delta = 0.0$) and coupling constants ($J$) are given in Hz. $^{31}$P NMR spectra were recorded on a Bruker 200 MHz operating at 81 MHz with 85% phosphoric acid ($\delta = 0.0$) as external standard. The ESI-HRMS was measured on Bruker APEX spectrometer in positive mode. IR spectra were recorded on AVATAR 360 ESP FTS spectrophotometer with KBr pellets. Melting points were determined with XRC-1 micro melting point apparatus and were uncorrected.

Cholic acid, deoxycholic acid, and diphenyl phosphite (DPP) were purchased from Sigma Company (Beijing-order Branch, People's Republic of China) and used without further purification. Pyridine was purchased from Beijing Chemicals Co. (Beijing, People's Republic of China) and redistilled prior to use. Cholic acid methyl ester (CAME, **3**) and deoxycholic acid methyl ester (DCAME, **7**) were prepared according to a previous reported procedure [19]. A typical procedure for the synthesis of bile acid derived *H*-phosphonates and phosphoramidate is represented by conjugates **5** and **12**, respectively.

### *Methyl 3α,7α,12α-tri(propargy-H-phosphonate)-5β-cholan-24-ate (**5**)*

Under an argon atmosphere, CAME (254 mg, 0.6 mmol) dissolved in pyridine (5 mL) was added dropwise to DPP (534 mg, 2.0 mmol) solution in 4 mL dry pyridine at −10°C. The resulting mixture was stirred at room temperature for 5 h, and propargyl alcohol (0.129 mL, 2.2 mmol) was syringed. After stirring for additional 7 h, the solvent was evaporated under vacuum and the obtained residue was purified on a column (silica gel; $CH_2Cl_2$: AcOEt = 7:2) to provide the desired product (244 mg, 0.34 mmol, light-yellow oil) in 56% yield. IR (cm$^{-1}$): 3449, 3293, 3228, 2947, 2946, 2873, 2434, 2125, 1735, 1251, 977; $^{31}$P NMR (81 MHz, $CDCl_3$): $\delta = 6.92$, 7.25, 7.99, 8.08; $^1$H NMR (600 MHz, $CDCl_3$): $\delta = 0.67$(s, 3H, 18-$CH_3$), 0.85 (s, 3H, 19-$CH_3$), 0.91–0.92 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 0.98–1.97 (m, 20H, aliphatic H), 2.14–2.32 (m, 4H, 2,4-$CH_2$), 2.56–2.64 (m, 3H, 3 × ≡C—H), 3.60 (s, 3H, $OCH_3$), 4.26 (m, 1H, 3α-CH), 4.59–4.68 (m, 7H, 3 × —C$H_2$C≡CH, 7α-CH), 4.80–4.84 (m, 1H, 12α-CH), 6.86 (d, 1H, $J = 710$ Hz, 3′-PH), 6.91, 6.93* (d, 1H, $J = 710$ Hz, 7′-PH), 6.96, 6.99* (d, 1H, $J = 710$ Hz, 12′-PH); HRMS (ESI) found: 946.2994, $[C_{34}H_{51}O_{11}P_3 + NH_4]^+$ calcd: 946.2982. (*The chemical shift of the diastereoisomer)

### *Methyl 3α,7α,12α-tri(isopropyl-H-phosphonate)-5β-cholan-24-ate (**6**)*

Yield: 52%; colorless oil; IR (cm$^{-1}$): 2940, 2872, 2424, 2338, 1735, 1376, 1256, 974; $^{31}$P NMR (81 MHz, $CDCl_3$): $\delta = 4.93$, 5.79, 6.33; $^1$H NMR (600 MHz, $CDCl_3$): $\delta = 0.66$ (s, 3H, 18-$CH_3$), 0.84 (s, 3H, 19-$CH_3$), 0.90–0.91 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 0.97–1.94 (m, 38H, aliphatic H), 2.14–2.32 (m, 4H, 2,4-$CH_2$), 3.59 (s, 3H, $OCH_3$), 4.04–4.09 (m, 1H, 3′-POCH), 4.21 (br, s, 1H, 3α-CH), 4.53–4.55 (m, 1H, 7α-CH), 4.63–4.70 (m, 2H, 7′,12′-POCH), 4.74–4.76 (m, 1H, 12α-CH), 6.75 (m, 3H, $J = 690$ Hz, 3 × PH); HRMS (ESI) found: 958.3910, $[C_{34}H_{63}O_{11}P_3 + NH_4]^+$ calcd: 958.3921.

### *Methyl 3α,12α-di(propargyl-H-phosphonate)-5β-deoxycholan-24-ate (**8**)*

Yield: 57%; light-yellow oil; IR (cm$^{-1}$): 3459, 3293, 3224, 2943, 2868, 2435, 2125, 1735, 1251, 976; $^{31}$P NMR (81 MHz, $CDCl_3$): $\delta = 6.94$, 7.94; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$(ppm) = 0.67 (s, 3H, 18-$CH_3$), 0.86 (s, 3H, 19-$CH_3$), 0.92 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 0.98–1.97 (m, 26H, aliphatic H), 2.57–2.61 (m, 2H, 2 × ≡C—H), 3.64 (s, 3H, $OCH_3$), 4.43 (br, s, 1H, 3α-CH), 4.64–4.69 (m, 4H, 2 × —C$H_2$C≡CH), 4.79–4.85 (m, 1H, 12α-CH), 6.86 (s, 1H, $J = 710$ Hz, 3′-PH), 7.00, 7.01* (d, 1H, $J = 710$ Hz, 12′-PH); ESI-MS (+): $m/z$ 633 $[M + Na]^+$, 649 $[M + K]^+$; HRMS (ESI) found: 628.3163, $[C_{31}H_{48}O_8P_2 + NH_4]^+$ calcd: 628.3163.

### *Methyl 3α,12α-di(isopropyl-H-phosphonate)-5β-deoxycholan-24-ate (**9**)*

Yield: 60%; colorless oil; IR (cm$^{-1}$): 2978, 2868, 2429, 1736, 1375, 1240, 965; $^{31}$P NMR (81 MHz, $CDCl_3$): $\delta = 5.19$, 6.20, 6.62; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 0.66$ (s, 3H, 18-$CH_3$), 0.84 (s, 3H, 19-$CH_3$), 0.91 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 0.96–2.10 (m, 38H, aliphatic H), 3.61 (s, 3H, $OCH_3$), 4.07–4.10 (m, 1H, 3′-POC$H_2$($CH_3$)$_2$), 4.36 (br, s, 1H, 3α-CH), (m, 1H, 12′-POC$H_2$($CH_3$)$_2$), 4.75–4.78 (br. s, 1H, 12α-CH), 6.77 (m, 2H, $J = 693$ Hz, 2 × PH); HRMS (ESI) found: 636.3789, $[C_{31}H_{56}O_8P_2 + NH_4]^+$ calcd: 636.3787.

*Methyl 3α,12α-di(3′-azido-3′-deoxythymidine-H-phosphonate)-5β-deoxycholan-24-ate (**10**)*

Yield: 48%; colorless solid; IR ($cm^{-1}$): 2949, 2870, 2108, 1693, 1253, 974; $^{31}P$ NMR (81 MHz, $CDCl_3$): $\delta = 7.38, 7.63, 8.13, 9.57$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 0.66$ (s, 3H, 18-$CH_3$), 0.83 (s, 3H, 19-$CH_3$), 0.91 (d, 3H, $J = 6$ Hz, 21-$CH_3$),1.10–1.90 (m, 28H, aliphatic H), 1.91 (s, 6H, AZT-$CH_3$), 2.05–2.45 (m, 6H, 23-$CH_2$, AZT-$CH_2$), 3.60 (s, 3H, $OCH_3$), 3.94–4.00 (m, 2H, 2×AZT-$CHN_3$), 4.20–4.40 (m, 7H, 3α-CH, 2×AZT-OCH, −$POCH_2$), 4.77–4.85 (br, m, 1H, 12α-CH), 5.92–6.00 (m, 2H, 2 × NCH), 6.86 (s, 1H, $J = 687$ Hz, 3′-PH), 6.89, 6.93* (d, 1H, $J = 687$ Hz, 12′-PH), 7.38–7.80 (2d, 2H, 2×−C*H*=C ($CH_3$)CO), 9.30–9.45 (br, d, 2×CONH); HRMS (ESI) found: 1050.4567, $[C_{45}H_{66}N_{10}O_{14}P_2 + NH_4]^+$ calcd: 1050.4573.

*Methyl 3α,12α-di(2′,3′-didehydro-2′,3′-dideoxythymidine-H-phosphonate)-5β-deoxycholan-24-ate (**11**)*

Yield 49%; colorless solid; IR ($cm^{-1}$): 2963, 1663, 1261, 1093, 1020, 800; $^{31}P$ NMR (81 MHz, $CDCl_3$): $\delta = 7.31, 7.76, 7.78, 8.86$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 0.60$ (s, 3H, 18-$CH_3$), 0.83 (s, 3H, 19-$CH_3$), 0.89 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 1.10–1.90 (m, 28H, aliphatic H), 1.86 (s, 6H, D4T-$CH_3$), 2.18–2.38 (m, 2H, 23-$CH_2$), 3.55 (s, 3H, $OCH_3$), 4.13–4.35 (m, 5H, 3α-CH, 2 × $POCH_2$), 4.79–4.85 (br, m, 1H, 12α-CH), 4.94–4.98 (d, 2H, 2 × $POCH_2CH$), 5.85–5.87 (2d, 2H, 2 × −CH=), 6.13–6.19 (2d, 2H, 2 × =C*H*CHN), 6.82 (s, 1H, $J = 690$ Hz, 3′-PH), 6.84, 6.87* (d, 1H, $J = 687$ Hz, 12′-PH), 6.90–6.92 (m, 2H, 2 × −CH=CHN*H*), 7.19 (br, s, 2 × −C*H*=), 9.39–9.43 (br, s, 2 × CONH); ESI-MS (+): *m/z* 969 $[M + Na]^+$; HRMS (ESI) found: 964.4237, $[C_{45}H_{64}N_4O_{14}P_2 + NH_4]^+$ calcd: 964.4233.

*Cholic Acid Phosphoramidate Conjugate (**12**)*

The compound **5** (291.2 mg, 0.4 mmol) in $CH_3CN$ (2 mL) was added dropwise to the solution of l-phenylalanine methyl ester hydrochloride (295 mg, 1.2 mmol) in $Et_3N$ (0.5 mL)–$CCl_4$ (0.5 mL)–$H_2O$ (0.1 mL)–$CH_3CN$ (4 mL) at 0°C. Then the resulting mixture was stirred at room temperature for 30 min and the solvent was concentrated under vacuum below 40°C. The obtained residue was purified on a column (silica gel; $CH_2Cl_2$:$CH_3OH$ = 20:1) to yield the corresponding phosphoramidate **12** (413 mg, 0.33 mmol, hygroscopic white solid) in 82% yield; Mp = 58–62°C; IR ($cm^{-1}$): 2961, 2925, 1734, 1260, 1018, 799; $^{31}P$ NMR (121 MHz, $CDCl_3$): $\delta = 7.19, 7.25, 7.30, 7.62, 8.19, 8.54$; $^1H$ NMR (600 MHz, $CDCl_3$): $\delta = 0.62$ (s, 3H, 18-$CH_3$), 0.80 (s, 3H, 19-$CH_3$), 0.92–0.93 (d, 3H, $J = 6$ Hz, 21-$CH_3$), 1.18–2.48 (m, 24H, aliphatic H), 2.39–2.45 (m, 3H, 3 × ≡C—H), 2.78–3.03 (m, 6H, 3×$PhCH_2$), 3.12–3.48 (m, 3H, 3 × NH), 3.56–3.68 (q, 12H, 4 × $OCH_3$), 4.00 (m, 1H, 3α-CH), 4.08–4.44 (m, 3H, 3 × C*H*NH), 4.50–4.58 (m, 6H, 3 × −C$H_2$C≡CH), 4.48, 4.55* (d, 1H, 7α-CH), 4.62, 4.68* (d, 1H, 12α-CH), 7.07–7.23 (m, 25H, Ar-H); HRMS (ESI) found: 1277.5357, $[C_{64}H_{84}N_3O_{17}P_3 + NH_4]^+$ calcd: 1277.5352.

## *REFERENCES*


[1] Sjövall, J. Lipids 2004, 39, 703–722.
[2] Enhsen, A.; Krame, W.; Wess, G. Drug Discovery Today 1998, 3, 409–418.
[3] Li, C. H.; Peters, A. S.; Meredith, E. L.; Allman, G. W.; Savage, P. B. J Am Chem Soc 1998, 120, 2961–2962.
[4] Li, Y.; Zhang, Z.; Ju, Y.; Zhao, C. Lett Org Chem 2007, 4, 414–418.
[5] Virtanen, E.; Kolehmainen, E. Eur J Org Chem 2004, 3385–3399.
[6] Ryu, E. H.; Yan, J.; Zhong, Z.; Zhao, Y. J Org Chem 2006, 71, 7205–7213.
[7] Amo, V.; Siracusa, L.; Markidis, T.; Baragana, B.; Bhattarai, K. M.; Galobardes, M.; Naredo, G.; Pérez-Payán, M. N.; Davis, A. P. Org Biomol Chem 2004, 2, 3320–3328.
[8] Davis, A. P.; Pérez-Payán M. N. Synlett 1999, 991–996.
[9] Taotafa, U.; McMullin, D. B.; Lee, S. C.; Hansen, L. D. Savage, P. B. Org Lett 2000, 2, 4117–4120.
[10] Hu, X.; Zhang, Z.; Zhang, X.; Li, Z. Y.; Zhu, X. X. Steroids 2005, 70, 531–537.
[11] Xue, C. B.; Yin, Y. W.; Zhao, Y. F. Tetrahedron Lett 1988, 29, 1145–1148.
[12] Xiao, Q.; Sun, J.; Sun, Q.; Ju, Y.; Zhao, Y. F.; Cui, Y. X. Synthesis 2003, 1, 107–111.
[13] Westheimer, F. H. Science 1987, 235, 1173–1178.
[14] Cardona, V. M. F.; Ayi, A. I.; Aubertin, A. M.; Guedj, R. Antivir Res 1999, 42, 189–196.
[15] Kers, I.; Cieslak, J.; Jankowska, J.; Kraszewski, A.; Stawinskiz J. Nucleosides Nucleotides Nucleic Acids 1999, 18, 1245–1246.
[16] Jankowska, J.; Sobkowski, M.; Stawinski, J.; Kraszrwski, A. Tetrahedron Lett 1994, 35, 3355–3358.
[17] Xiao, Q.; Sun, J.; Ju, Y.; Zhao, Y. F.; Cui, Y. X. Chem Lett 2003, 32, 522–523.
[18] Sobkowski, M.; Jankowska, J.; Stawinksi, J.; Kraszewski, A. Nucleosides Nucleotides Nucleic Acids 2005, 24, 1033–1036.
[19] Gouin, S.; Zhu, X. X. Steroids 1996, 61, 664–669.