

Green synthesis of novel phosphonate derivatives using ultrasonic irradiation

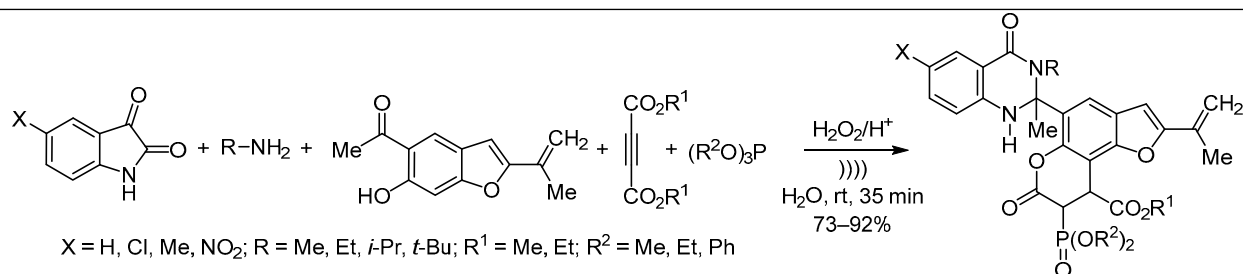
Shirin Sharafian¹, Zinatossadat Hossaini^{1*},
Faramarz Rostami-Charati^{1,2}, Mohammad A. Khalilzadeh¹

¹ Department of Chemistry, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran; e-mail: zshossaini@yahoo.com

² Research Center for Conservation of Culture Relics, Research Institute of Cultural Heritage & Tourism, Tehran, Iran

Published in Khimiya Geterotsiklicheskih Soedinenii, 2020, 56(10), 1283–1291

Submitted November 25, 2019
Accepted after revision July 9, 2020



A novel and efficient procedure for the generation of quinazolinone phosphonate derivatives employing the reaction of euparin, isatin or its derivatives, primary amines, dialkyl acetylenedicarboxylates, trimethyl phosphite or triphenyl phosphite, and acidic solution of hydrogen peroxide in aqueous media at ambient temperature under ultrasonic irradiation was developed. Without ultrasonic irradiation, the reaction does not proceed and agitation of the reaction mixture is difficult. Some advantages of this procedure are: short time of reaction, high yields of products, easy isolation of products.

Keywords: euparin, isatin, primary amines, multicomponent reaction, ultrasonic irradiation.

Many diverse sonochemistry-based procedures have been developed recently.¹ Sonochemistry is as an original and valuable method attracting increasing interest for accelerating organic reactions.^{2–5} Luche and coworkers have carried out a number of investigations which provided the basis for using sonochemistry in organic synthesis^{6–9} offering significant features for organic reactions such as improvement of reaction rates, formation of pure products with high yields and easier process, energy saving, and waste decreasing when compared with traditional methods.^{10,11} In our previous work,¹² we prepared phosphonate in H₂O under conventional conditions at high temperature and with long reaction time, but under ultrasonic irradiation we managed to improve the course of the reaction in H₂O in terms of chemoselectivity and economic issues.^{12,13}

On the other hand, optically active phosphonates are valuable compounds,^{14,15} displaying wide range of biological activity, including anti-influenza,¹⁶ antipsoriatic,¹⁷ antibiotic,¹⁸ antibacterial,¹⁹ enzyme inhibiting,²⁰ and herbicidal.^{21–23} Many approaches to the synthesis of

organophosphorus compounds exist and are described in current literature.^{24–31}

Another structural moiety that was targeted in this study was quinazolinone framework. Quinazolinones are important compounds with pharmacological and biological activities such as antifungal,³² antibacterial,³³ and antitumor.³⁴ Because of these important properties, different procedures have been reported in literature for producing quinazolinone derivatives.^{35–41}

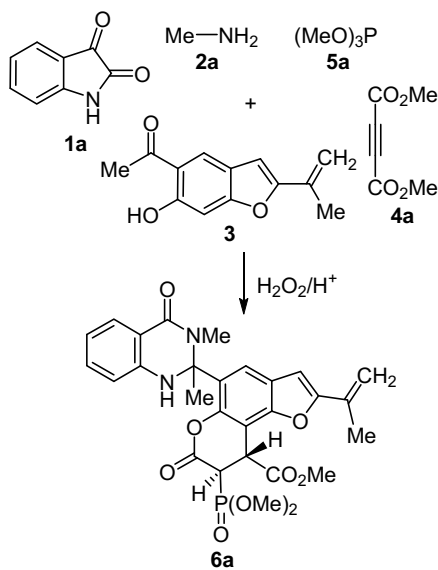
Herein, in continuation of previous works^{42,43} and our studies for discovering new synthetic methodologies, in this research, a series of novel phosphonate derivatives containing quinazolinone **6** were synthesized in excellent yields and short reaction time using the reaction of isatin or its derivatives **1**, primary amines **2**, euparin (**3**),⁴² dialkyl acetylenedicarboxylates **4**, trimethyl phosphite or triphenyl phosphite **5** in the presence of acidic solution of hydrogen peroxide. Initially, for determination of the best conditions for generation of compound **6a**, the reaction of isatin **1a**, methylamine (**2a**), euparin (**3**),⁴² dimethyl acetylenedicarboxylate (**4a**), and trimethyl phosphite (**5a**) in the

presence of acidic solution of H_2O_2 was selected as a model reaction (Table 1).⁴³

Optimum conditions for the product **6a** generation were found by varying solvent and temperature. For this purpose, the model reaction was performed under conventional and ultrasonic irradiation conditions in CH_2Cl_2 , MeCN, CHCl_3 , H_2O , PhMe, DMF, and using solvent-free conditions (Table 1). Finally, excellent yields of compound **6a** were obtained in H_2O under ultrasonic irradiation at room temperature as the best found conditions.

The structure of compound **6a** was confirmed by IR, ^1H , ^{13}C NMR, and mass spectral data. The ^1H NMR spectrum of compound **6a** displays three singlets at 1.75, 2.15, and 2.56 ppm for methyl protons and one singlet at 3.69 ppm for methoxy protons. The methoxy groups of the phosphoranyl moiety are diastereotopic and display two doublets at 3.85 and 3.92 ppm. Two doublet doublets represent vicinal methine protons at 3.78 and 4.68 ppm. The NH group appeared at 6.23 ppm along with signals of aromatic moiety at lower fields. In the ^{13}C NMR spectrum, the resonances related to 28 carbon atoms of compound **6a**

Table 1. Optimization of the reaction conditions for the synthesis of compound **6a**



Solvent	Temperature, °C	Conventional conditions		Ultrasonic irradiation	
		Time, h	Yield, %	Time, h	Yield, %
–	rt	12	–	2	35
H₂O	rt	12	15	1	95
MeCN	rt	10	20	2	85
PhMe	rt	10	15	3	80
CH_2Cl_2	rt	10	15	2	85
CHCl_3	rt	12	20	2	90
DMF	rt	12	–	5	25
–	90	12	–	2	38
H_2O	90	12	18	1	97
MeCN	90	10	24	2	88
PhMe	90	10	18	3	83
CH_2Cl_2	90	10	19	2	87
CHCl_3	90	12	19	2	92
DMF	90	12	–	5	28

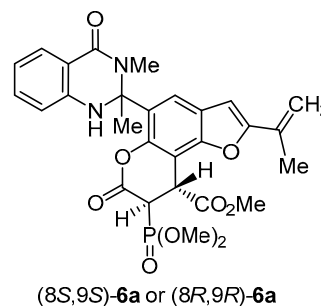
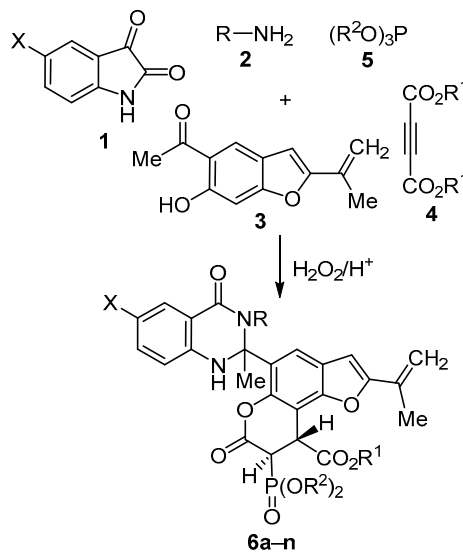


Figure 1. Diastereoisomer with *anti* HCCH arrangements.

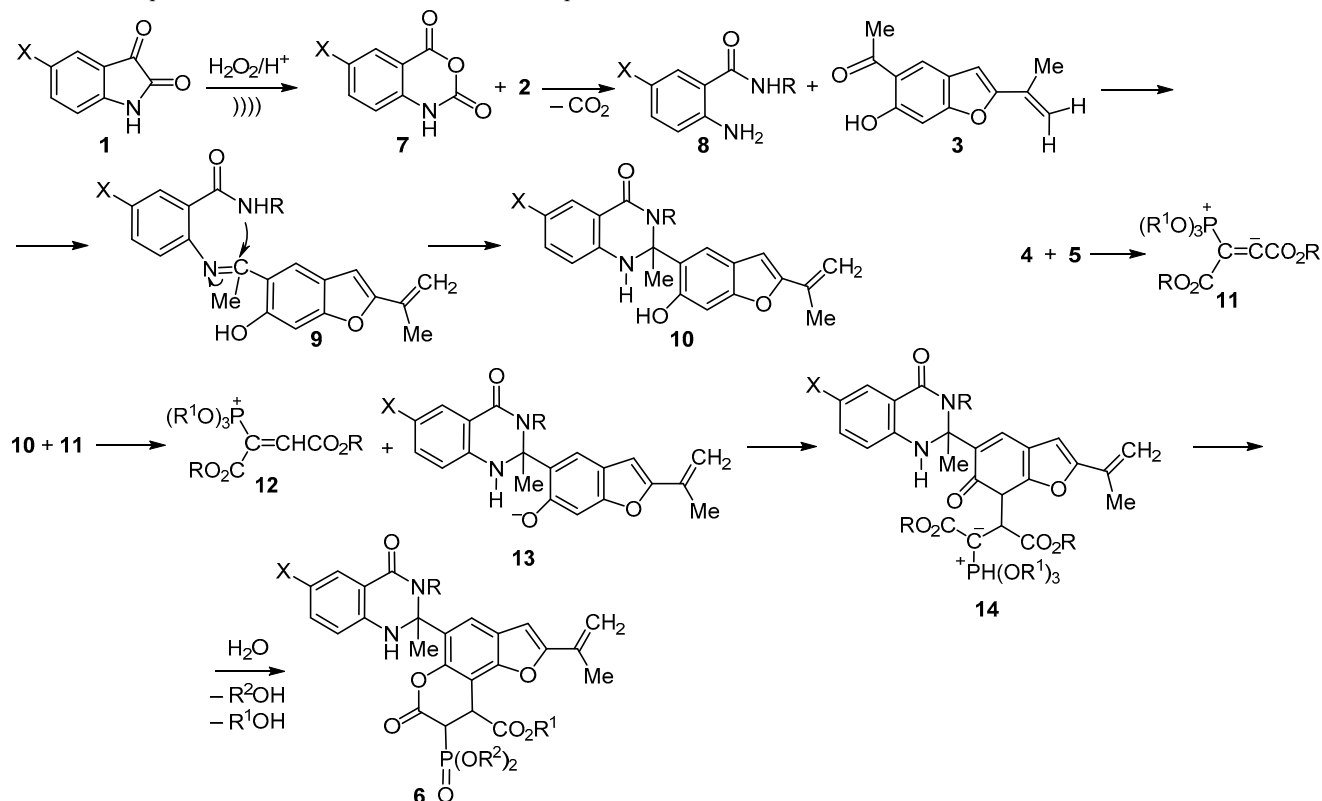
appeared in agreement with the proposed structure. Observation of $^3J_{\text{HH}} = 11.6$ Hz for the vicinal methine protons in compound **6a** indicates the dominance of *anti* arrangement (Fig. 1). Also, the observation of $^3J_{\text{CP}}$ of 22.5 Hz for the CO_2Me group and $^3J_{\text{CP}}$ of zero for the C atom of benzene ring is in agreement with the (8*S*,9*S*)- or (8*R*,9*R*)-diastereoisomer.^{27c,44}

The next step after optimization of the synthesis of euparin-based quinazolinone **6a** was the synthesis of the number of its substituted derivatives **6b–n** (Table 2).

Table 2. Green synthesis of euparin-based quinazolinones **6a–n** under ultrasonic irradiation



Compound	R	R ¹	R ²	X	Yield, %
6a	Me	Me	Me	H	95
6b	Et	Me	Me	H	87
6c	<i>t</i> -Bu	Me	Me	H	85
6d	<i>i</i> -Pr	Me	Me	H	82
6e	Me	Et	Me	H	87
6f	Me	Me	Ph	H	80
6g	Me	Me	Et	H	85
6h	Et	Me	Et	H	87
6i	<i>t</i> -Bu	Et	Ph	H	73
6j	Me	Me	Me	Me	92
6k	Et	Me	Me	Me	90
6l	<i>t</i> -Bu	Me	Me	NO_2	85
6m	<i>i</i> -Pr	Me	Me	Cl	87
6n	Me	Me	Ph	Me	87

Scheme 1. Proposed mechanism for the formation of compounds **6**

The putative mechanism of the reaction is shown in Scheme 1. According to the proposed mechanism, isatin **1** undergoes Baeyer–Villiger oxidation with H_2O_2 in acidic solution under ultrasonic irradiation to produce isatoic anhydride **7**. Isatoic anhydride **7** and primary amines **2** react to generate anthranilamide **8** with elimination of CO_2 . Condensation of euparin (**3**)⁴² with intermediate **8** produces quinazolinone **10** with intermediacy of imine **9** under ultrasonic irradiation. It should be noted that intramolecular cyclization does not proceed without ultrasonic irradiation. According to the known chemistry of phosphorus nucleophiles,^{45,46} the addition of phosphite **5** to activated acetylenic compounds **4** produces compound **11** that deprotonates quinazolinone **10** to generate intermediates **12** and **13**. Further Michael addition of phenolate anion **13** to vinylphosphonium salt **12**, cyclization of intermediate **14**, and hydrolysis of quasiphosphonium salt completes the formation of final product **6**.

Under similar conditions, a series of novel phosphonate derivatives containing quinazolinone framework **16** were synthesized by the reaction of isatins **1**, primary amines **2**, 2'-hydroxyacetophenones or salicylaldehydes **15**, dialkyl acetylenedicarboxylates **4**, trimethyl phosphite or triphenyl phosphite **5** in the presence of acidic solution of hydrogen peroxide at ambient temperature under ultrasonic irradiation in excellent yields and short reaction time (Table 3).

The structures of compounds **16** were confirmed by IR, ^1H , ^{13}C NMR, and mass spectral data. For example, the ^1H NMR spectrum of compound **16a** showed two singlets at 1.65 and 2.58 ppm for methyl protons and one singlet at 3.75 ppm for methoxy protons. Two methoxy groups of the phosphoranyl moiety are diastereotopic and showed two

Table 3. Green synthesis of quinazolinone phosphonate derivatives **16a–h**

Compound	R	R ¹	X	X ¹	X ²	Yield, %
16a	Me	Me	H	H	H	97
16b	Et	Me	H	MeO	H	95
16c	<i>t</i> -Bu	Me	Me	MeO	H	95
16d	<i>i</i> -Pr	Me	NO ₂	H	Me	90
16e	Me	H	H	H	H	97
16f	Et	H	H	MeO	H	95
16g	<i>t</i> -Bu	H	Me	MeO	H	95
16h	<i>i</i> -Pr	H	NO ₂	H	MeO	90

doublets at 3.87 and 3.93 ppm. Two doublet doublets represent vicinal methine protons at 3.83 and 4.72 ppm. The NH group appeared at 6.18 ppm along with signals for aromatic moiety. In the ^{13}C NMR spectrum of compound **16a**, the resonances related to three carbonyl groups appeared at 160.3 (C=O), 161.3 (d, $^2J_{\text{PC}} = 6.8$ Hz, C=O), 167.5 ppm (d, $^3J_{\text{PC}} = 22.5$ Hz, C=O).

^1H NMR spectrum of compound **16e** exhibited two singlets at 3.48 and 3.75 ppm for NMe and methoxy protons, respectively. The methoxy groups of the phosphoranyl moiety are diastereotopic because of stereogenic center and display two doublets at 3.89 and 3.95 ppm and two doublet doublets for vicinal methine protons at 3.83 and 4.74 ppm along with signals for aromatic moiety. In the ^{13}C NMR spectrum of compound **16e**, the resonances related to three carbonyl group appeared at 160.5, 161.6, 168.2 ppm.

In conclusion, in this research we described green, one-pot procedure for the synthesis of novel quinazolinone phosphonate derivatives starting from isatins, primary amine, euparin, 2-hydroxyacetophenone or its derivatives, 2-hydroxybenzaldehyde or its derivatives, activated acetylenic compounds, and trimethyl phosphite or triphenyl phosphite in the presence of acidic solution of H_2O_2 in water at room temperature under ultrasonic irradiation. This transformation proceeds only under ultrasonic irradiation and features excellent yields, short reaction time, high atom economy, and mild reaction conditions.

Experimental

IR spectra were recorded on a Shimadzu IR-460 spectrometer in KBr pellets. ^1H , ^{13}C , and ^{31}P NMR spectra were recorded on a Bruker Avance DRX-500 spectrometer (500, 126, and 202 MHz, respectively) in CDCl_3 solutions using TMS as internal standard or 85 mass % H_3PO_4 as external standard. The electron ionization mass spectra were recorded on a Finnigan MAT-8430 spectrometer operating at an ionization potential of 70 eV. The elemental analyses were performed on a Heraeus CHNO-Rapid analyzer. Melting points were measured on Electrothermal 9100 apparatus.

All the chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and used without further purification.

Preparation of 1-(6-hydroxy-2-isopropenyl-1-benzofuranyl)-1-ethanone (3). Dry, powdered rhizomes of *Petasites hybridus* (950 g) were extracted with THF–MeOH, 1:1 mixture. Evaporation of the solvent under reduced pressure and washing with cold Et_2O gave euparin (**3**) as yellow solid.

Synthesis of compounds 6a–n, 16a–h (General method). A mixture of 1*H*-indole-2,3-dione **1** (2 mmol), AcOH (1 ml), 5 drops of concentrated H_2SO_4 and 20% (wt%) H_2O_2 were sonicated at room temperature for 10 min in a beaker equipped with ultrasonic probe under the power of 60 W. After 10 min, anhydrous primary amine **2** (2 mmol) was added. After 5 min, 1-(6-hydroxy-2-isopropenyl-1-benzofuranyl)-1-ethanone (euparin) (**3**) (2 mmol), or 1-(2-hydroxyphenyl)ethanone, or 2-hydroxybenzaldehyde **15** was added under ultrasonic irradiation. Dialkyl acety-

lenedicarboxylate **4** (2 mmol) and trimethyl phosphite or triphenyl phosphite **5** (2 mmol) were added after 10 min. Reaction completion at every stage was monitored by TLC employing 5:1 EtOAc–*n*-hexane as an eluent. After completion of the procedure, formed precipitate was filtered off and washed with Et_2O to afford pure title compound **6a–n** or **16a–h**.

Methyl (8*R*,9*R*)-8-(dimethoxyphosphoryl)-5-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6a). Yield 1.04 g (95%), yellow powder, mp 193–195°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1695, 1625, 1585, 1468, 1375, 1294. ^1H NMR spectrum, δ , ppm (*J*, Hz): 1.75 (3H, s, CH_3); 2.15 (3H, s, CH_3); 2.56 (3H, s, CH_3); 3.69 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.78 (1H, dd, $^2J_{\text{HP}} = 19.8$, $^3J_{\text{HH}} = 11.6$, PCCH); 3.85 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.92 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.68 (1H, dd, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{HP}} = 9.5$, PCCH); 4.75 (1H, d, $^2J = 4.2$, C=CH); 5.12 (1H, d, $^2J = 4.2$, C=CH); 6.23 (1H, s, NH); 6.95 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.15 (1H, t, $^3J_{\text{HH}} = 7.8$, H Ar); 7.23 (1H, t, $^3J_{\text{HH}} = 7.8$, H Ar); 7.43 (1H, s, H Ar); 7.52 (1H, s, H Ar); 7.93 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar). ^{13}C NMR spectrum, δ , ppm (*J*, Hz): 18.5; 25.3; 34.2; 42.3 (d, $^2J_{\text{PC}} = 9.3$); 46.3 (d, $J = 143.2$); 51.2 (d, $J = 8.7$); 52.4 (d, $^2J_{\text{PC}} = 8.7$); 52.8; 76.4; 105.2; 113.2; 114.2; 114.8; 121.6; 122.3; 122.4; 124.3; 125.2; 127.4; 133.6; 137.6; 142.3; 151.8; 152.3; 154.3; 160.3; 161.3 (d, $J = 6.8$); 167.5 (d, $J = 22.5$). ^{31}P NMR spectrum, δ , ppm: 19.6. Mass spectrum, m/z (I_{rel} , %): 568 [M] $^+$ (10), 537 (92), 31 (100). Found, %: C 59.34; H 5.28; N 5.14. $\text{C}_{28}\text{H}_{29}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 59.16; H 5.14; N 4.93.

Methyl (8*R*,9*R*)-8-(dimethoxyphosphoryl)-5-(3-ethyl-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6b). Yield 1.01 g (87%), yellow powder, mp 201–203°C. IR spectrum, ν , cm^{-1} : 1739, 1735, 1697, 1635, 1587, 1475, 1382, 1293. ^1H NMR spectrum, δ , ppm (*J*, Hz): 1.25 (3H, t, $^3J_{\text{HH}} = 7.3$, CH_2CH_3); 1.73 (3H, s, CH_3); 2.16 (3H, s, CH_3); 2.75–2.83 (1H, m, CH); 3.12–3.22 (1H, m, CH); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.82 (1H, dd, $^2J_{\text{HP}} = 19.5$, $^3J_{\text{HH}} = 11.5$, PCCH); 3.89 (3H, d, $^3J_{\text{HP}} = 11.7$, CH_3OP); 3.95 (3H, d, $^3J_{\text{HP}} = 11.7$, CH_3OP); 4.74 (1H, dd, $^3J_{\text{HP}} = 10.2$, $^3J_{\text{HH}} = 11.5$, PCCH); 4.83 (1H, d, $^2J = 4.5$, C=CH); 5.23 (1H, d, $^2J = 4.5$, C=CH); 6.18 (1H, s, NH); 7.02 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.18 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.28 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.47 (1H, s, H Ar); 7.54 (1H, s, H Ar); 7.87 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (*J*, Hz): 14.2; 18.7; 25.4; 40.2; 42.5 (d, $J = 9.7$); 45.8 (d, $J = 145.2$); 51.2 (d, $J = 9.2$); 52.5 (d, $J = 9.2$); 53.4; 76.5; 106.2; 113.5; 114.3; 114.5; 121.7; 122.5; 122.9; 124.2; 125.3; 127.6; 132.8; 137.5; 142.4; 151.6; 152.6; 154.5; 160.5; 161.7 (d, $J = 7.3$); 168.2 (d, $J = 22.4$). ^{31}P NMR spectrum, δ , ppm: 20.3. Mass spectrum, m/z (I_{rel} , %): 582 [M] $^+$ (15), 551 (86), 31 (100). Found, %: C 59.93; H 5.52; N 4.96. $\text{C}_{29}\text{H}_{31}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 59.79; H 5.36; N 4.81.

Methyl (8*R*,9*R*)-5-[3-(*tert*-butyl)-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl]-8-(dimethoxyphosphoryl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6c). Yield 1.04 g (85%), yellow powder, mp 215–217°C. IR spectrum, ν , cm^{-1} : 1740, 1737, 1698, 1642, 1576, 1478, 1376, 1284. ^1H NMR spectrum, δ , ppm

(*J*, Hz): 1.16 (9H, s, C(CH₃)₃); 1.68 (3H, s, CH₃); 2.18 (3H, s, CH₃); 3.72 (3H, s, C(O)OCH₃); 3.83 (1H, dd, ²*J*_{HP} = 20.4, ³*J*_{HH} = 12.2, PCH); 3.87 (3H, d, ³*J*_{HP} = 11.8, CH₃OP); 3.95 (3H, d, ³*J*_{HP} = 11.8, CH₃OP); 4.73 (1H, d, ²*J*_{HH} = 4.7, C=CH); 4.86 (1H, dd, ³*J*_{HH} = 12.2, ³*J*_{HP} = 9.8, PCCH); 5.15 (1H, d, ²*J*_{HH} = 4.7, C=CH); 6.25 (1H, s, NH); 7.04 (1H, d, ³*J*_{HH} = 7.6, H Ar); 7.18 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.25 (1H, t, ³*J*_{HH} = 7.7, H Ar); 7.45 (1H, s, H Ar); 7.56 (1H, s, H Ar); 8.02 (1H, d, ³*J*_{HH} = 7.7, H Ar). ¹³C NMR spectrum, δ, ppm (*J*, Hz): 18.6; 27.5; 31.4; 42.7 (d, *J* = 10.2); 47.4 (d, *J* = 147.3); 51.5 (d, *J* = 9.5); 52.3 (d, *J* = 9.5); 52.8; 62.3; 77.4; 113.3; 114.2; 114.5; 115.3; 116.3; 123.2; 123.6; 124.5; 125.8; 127.6; 134.3; 137.2; 142.5; 152.3; 152.8; 154.8; 160.8; 161.6 (d, *J* = 6.5); 169.4 (d, *J* = 21.8). ³¹P NMR spectrum, δ, ppm: 21.6. Mass spectrum, *m/z* (*I*_{rel}, %): 610 [M]⁺ (10), 553 (86), 57 (100), 31 (100). Found, %: C 61.16; H 5.89; N 4.78. C₃₁H₃₅N₂O₉P. Calculated, %: C 60.98; H 5.78; N 4.59.

Methyl (8*R*,9*R*)-8-(dimethoxyphosphoryl)-2-isopropenyl-5-(3-isopropyl-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6d). Yield 0.98 g (82%), yellow powder, mp 209–211°C. IR spectrum, ν, cm^{−1}: 1738, 1736, 1695, 1658, 1586, 1484, 1375, 1293. ¹H NMR spectrum, δ, ppm (*J*, Hz): 1.12 (6H, d, ³*J*_{HH} = 6.7, 2CH₃); 1.76 (3H, s, CH₃); 2.16 (3H, s, CH₃); 3.68 (3H, s, C(O)OCH₃); 3.74–3.85 (2H, m, 2CH); 3.89 (3H, d, ³*J*_{HP} = 12.2, CH₃OP); 3.96 (3H, d, ³*J*_{HP} = 12.2, CH₃OP); 4.75 (1H, d, ²*J* = 4.8, C=CH); 4.87 (1H, dd, ³*J*_{HH} = 12.0, ³*J*_{HP} = 10.3, PCCH); 5.09 (1H, d, ²*J* = 4.8, C=CH); 6.22 (1H, s, NH); 7.08 (1H, d, ³*J*_{HH} = 7.5, H Ar); 7.23 (1H, t, ³*J*_{HH} = 7.5, H Ar); 7.32 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.48 (1H, s, H Ar); 7.62 (1H, s, H Ar); 8.04 (1H, d, ³*J*_{HH} = 7.6, H Ar). ¹³C NMR spectrum, δ, ppm (*J*, Hz): 18.5; 22.4; 26.4; 42.3 (d, *J* = 10.5); 43.5; 47.6 (d, *J* = 148.6); 51.7 (d, *J* = 10.2); 52.5 (d, *J* = 10.2); 53.2; 76.2; 105.3; 113.3; 114.3; 114.7; 121.4; 122.2; 122.5; 125.4; 125.8; 127.4; 133.6; 137.2; 142.2; 151.8; 153.2; 154.4; 161.2; 162.3 (d, *J* = 6.7); 170.3 (d, *J* = 22.3). ³¹P NMR spectrum, δ, ppm: 22.3. Mass spectrum, *m/z* (*I*_{rel}, %): 596 [M]⁺ (15), 565 (84), 31 (100). Found, %: C 60.58; H 5.74; N 4.86. C₃₀H₃₃N₂O₉P. Calculated, %: C 60.40; H 5.58; N 4.70.

Ethyl (8*R*,9*R*)-8-(dimethoxyphosphoryl)-5-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6e). Yield 1.01 g (87%), yellow powder, mp 186–188°C. IR spectrum, ν, cm^{−1}: 1740, 1737, 1698, 1634, 1587, 1476, 1378, 1297. ¹H NMR spectrum, δ, ppm (*J*, Hz): 1.23 (3H, t, ³*J*_{HH} = 7.4, CH₂CH₃); 1.72 (3H, s, CH₃); 2.18 (3H, s, CH₃); 2.48 (3H, s, CH₃); 3.75 (1H, dd, ²*J*_{HP} = 19.5, ³*J*_{HH} = 11.6, PCH); 3.83 (3H, d, ³*J*_{HP} = 11.3, CH₃OP); 3.87 (3H, d, ³*J*_{HP} = 11.3, CH₃OP); 4.12 (2H, q, ³*J*_{HH} = 7.4, CH₂CH₂O); 4.65 (1H, dd, ³*J*_{HH} = 11.6, ³*J*_{HP} = 9.8, PCCH); 4.78 (1H, d, ²*J*_{HH} = 3.8, C=CH); 5.16 (1H, d, ²*J*_{HH} = 3.8, C=CH); 6.16 (1H, s, NH); 6.92 (1H, d, ³*J*_{HH} = 7.6, H Ar); 7.12 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.24 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.38 (1H, s, H Ar); 7.43 (1H, s, H Ar); 7.87 (1H, d, ³*J*_{HH} = 7.6, H Ar). ¹³C NMR spectrum, δ, ppm (*J*, Hz): 14.2; 18.3; 24.8; 34.5; 42.5 (d, *J* = 9.7); 46.8 (d, *J* = 147.4); 51.3 (d, *J* = 9.2); 52.3 (d, *J* = 9.2); 61.2; 78.3; 105.4; 112.8; 113.6; 114.2; 121.3; 122.5; 125.3; 125.8; 127.3; 133.2; 137.2; 142.5; 151.6;

153.4; 154.4; 160.5; 161.8 (d, *J* = 7.3); 168.4 (d, *J* = 21.8). ³¹P NMR spectrum, δ, ppm: 19.8. Mass spectrum, *m/z* (*I*_{rel}, %): 582 [M]⁺ (15), 537 (76), 45 (100). Found, %: C 59.93; H 5.52; N 4.96. C₂₉H₃₁N₂O₉P. Calculated, %: C 59.79; H 5.36; N 4.81.

Methyl (8*R*,9*R*)-5-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-8-(diphenoxyphosphoryl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6f). Yield 1.07g (80%), pale-yellow powder, mp 216–218°C. IR spectrum, ν, cm^{−1}: 1745, 1742, 1698, 1667, 1589, 1486, 1385, 1297. ¹H NMR spectrum, δ, ppm (*J*, Hz): 1.65 (3H, s, CH₃); 2.14 (3H, s, CH₃); 2.48 (3H, s, CH₃); 3.68 (3H, s, C(O)OCH₃); 4.25 (1H, dd, ²*J*_{HP} = 19.5, ³*J*_{HH} = 11.8, PCH); 4.86 (1H, dd, ³*J*_{HH} = 11.8, ³*J*_{HP} = 10.4, PCCH); 4.93 (1H, d, ²*J*_{HH} = 4.8, C=CH); 5.23 (1H, d, ²*J*_{HH} = 4.8, C=CH); 6.32 (1H, s, NH); 6.86 (1H, d, ³*J*_{HH} = 7.6, H Ar); 7.12 (2H, d, ³*J*_{HH} = 7.5, H Ar); 7.16 (2H, d, ³*J*_{HH} = 7.5, H Ar); 7.22 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.28 (1H, t, ³*J*_{HH} = 7.5, H Ar); 7.32 (1H, t, ³*J*_{HH} = 7.5, H Ar); 7.37 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.42 (2H, t, ³*J*_{HH} = 7.5, H Ar); 7.48 (2H, t, ³*J*_{HH} = 7.5, H Ar); 7.52 (1H, s, H Ar); 7.58 (1H, s, H Ar); 7.96 (1H, d, ³*J*_{HH} = 7.6, H Ar). ¹³C NMR spectrum, δ, ppm (*J*, Hz): 18.7; 24.6; 34.5; 37.8 (d, *J* = 9.6); 40.2 (d, *J* = 158.3); 51.6; 77.8; 107.2; 113.4; 114.2; 115.3; 120.5 (d, *J* = 23.4); 121.6 (d, *J* = 23.4); 122.5; 123.2; 123.5; 125.3; 125.8; 126.3; 127.4; 128.3; 128.8; 133.5; 137.5; 142.6; 151.3 (d, *J* = 10.4); 151.8 (d, *J* = 10.4); 152.2; 153.6; 154.5; 159.4; 160.8 (d, *J* = 7.3); 165.6 (d, *J* = 22.8). ³¹P NMR spectrum, δ, ppm: 19.6. Mass spectrum, *m/z* (*I*_{rel}, %): 692 [M]⁺ (10), 661 (68), 31 (100). Found, %: C 66.04; H 4.95; N 4.22. C₃₈H₃₃N₂O₉P. Calculated, %: C 65.89; H 4.80; N 4.04.

Methyl (8*R*,9*R*)-8-(diethoxyphosphoryl)-5-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6g). Yield 1.01 g (85%), yellow powder, mp 198–200°C. IR spectrum, ν, cm^{−1}: 1739, 1737, 1696, 1647, 1587, 1465, 1376, 1297. ¹H NMR spectrum, δ, ppm (*J*, Hz): 1.18 (3H, t, ³*J*_{HH} = 7.4, OCH₂CH₃); 1.23 (3H, t, ³*J*_{HH} = 7.4, OCH₂CH₃); 1.72 (3H, s, CH₃); 2.16 (3H, s, CH₃); 2.47 (3H, s, CH₃); 3.68 (3H, s, C(O)OCH₃); 3.82 (1H, dd, ²*J*_{HP} = 20.4, ³*J*_{HH} = 12.3, PCH); 3.92–4.05 (2H, m, OCH₂CH₂); 4.12–4.22 (2H, m, OCH₂CH₂); 4.87 (1H, dd, ³*J*_{HH} = 12.3, ³*J*_{HP} = 10.3, PCCH); 4.93 (1H, d, ²*J*_{HH} = 5.4, C=CH); 5.16 (1H, d, ²*J*_{HH} = 5.4, C=CH); 6.28 (1H, s, NH); 7.08 (1H, d, ³*J*_{HH} = 7.7, H Ar); 7.16 (1H, t, ³*J*_{HH} = 7.6, H Ar); 7.26 (1H, t, ³*J*_{HH} = 7.5, H Ar); 7.52 (1H, s, H Ar); 7.63 (1H, s, H Ar); 8.04 (1H, d, ³*J*_{HH} = 7.6, H Ar). ¹³C NMR spectrum, δ, ppm (*J*, Hz): 15.2 (d, *J* = 8.2); 16.4 (d, *J* = 8.2); 18.7; 24.8; 34.7; 42.5 (d, *J* = 9.8); 47.2 (d, *J* = 156.4); 51.4; 62.4 (d, *J* = 9.3); 63.2 (d, *J* = 9.3); 77.3; 105.6; 113.4; 113.8; 114.2; 122.3; 123.4; 123.8; 124.8; 125.6; 127.6; 133.8; 137.2; 142.6; 152.3; 153.4; 154.5; 161.2; 162.4 (d, *J* = 6.5); 168.2 (d, *J* = 21.8). ³¹P NMR spectrum, δ, ppm: 20.3. Mass spectrum, *m/z* (*I*_{rel}, %): 596 [M]⁺ (15), 551 (68), 45 (100), 31 (100). Found, %: C 60.58; H 5.76; N 4.87. C₃₀H₃₃N₂O₉P. Calculated, %: C 60.40; H 5.58; N 4.70.

Ethyl (8*R*,9*R*)-8-(diethoxyphosphoryl)-5-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate

(6h). Yield 1.06 g (87%), yellow powder, mp 203–205°C. IR spectrum, ν , cm^{-1} : 1745, 1739, 1698, 1652, 1583, 1468, 1386, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.15 (3H, t, $^3J_{\text{HH}} = 7.4$, OCH_2CH_3); 1.25 (3H, t, $^3J_{\text{HH}} = 7.4$, OCH_2CH_3); 1.34 (3H, t, $^3J_{\text{HH}} = 7.5$, NCH_2CH_3); 1.78 (3H, s, CH_3); 2.14 (3H, s, CH_3); 2.45–2.58 (2H, m, NCH_2CH_3); 3.72 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.84 (1H, dd, $^2J_{\text{HP}} = 19.4$, $^3J_{\text{HH}} = 11.2$, PCH); 3.95–4.09 (2H, m, OCH_2CH_3); 4.15–4.26 (2H, m, OCH_2CH_3); 4.65 (1H, dd, $^3J_{\text{HH}} = 11.2$, $^3J_{\text{HP}} = 10.5$, PCCH); 4.84 (1H, d, $^2J_{\text{HH}} = 5.8$, $\text{C}=\text{CH}$); 5.03 (1H, d, $^2J_{\text{HH}} = 5.8$, $\text{C}=\text{CH}$); 6.32 (1H, s, NH); 7.02 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.15 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.32 (1H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.46 (1H, s, H Ar); 7.58 (1H, s, H Ar); 7.89 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 14.2; 14.8 (d, $J = 9.4$); 15.6 (d, $J = 9.4$); 18.6; 25.4; 40.2; 41.6 (d, $J = 11.2$); 47.5 (d, $J = 155.8$); 51.6; 61.8 (d, $J = 9.8$); 62.6 (d, $J = 9.8$); 76.3; 106.4; 113.6; 114.3; 114.8; 121.4; 122.3; 123.2; 124.8; 125.8; 128.2; 133.4; 137.6; 143.2; 151.6; 152.8; 154.3; 160.8; 161.6 (d, $J = 8.3$); 169.4 (d, $J = 22.3$). ^{31}P NMR spectrum, δ , ppm: 23.4. Mass spectrum, m/z (I_{rel} , %): 610 $[\text{M}]^+$ (10), 565 (54), 45 (100), 31 (100). Found, %: C 60.63; H 5.92; N 4.76. $\text{C}_{31}\text{H}_{35}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 60.48; H 5.78; N 4.59.

Ethyl (8R,9R)-5-[3-(*tert*-butyl)-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl]-8-(diphenoxyphosphoryl)-2-isopropenyl-7-oxo-8,9-dihydro-7H-furo[2,3-*f*]chromene-9-carboxylate (6i). Yield 1.09 g (73%), pale-yellow powder, mp 221–223°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1697, 1675, 1587, 1487, 1387, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.23 (9H, s, $(\text{CH}_3)_3\text{C}$); 1.28 (3H, t, $^3J_{\text{HH}} = 7.4$, OCH_2CH_3); 1.67 (3H, s, CH_3); 2.15 (3H, s, CH_3); 4.12 (2H, q, $^3J_{\text{HH}} = 7.4$, OCH_2CH_3); 4.27 (1H, dd, $^2J_{\text{HP}} = 19.8$, $^3J_{\text{HH}} = 12.0$, PCH); 4.90 (1H, dd, $^3J_{\text{HH}} = 12.0$, $^3J_{\text{HP}} = 10.7$, PCCH); 4.97 (1H, d, $^2J_{\text{HH}} = 4.2$, $\text{C}=\text{CH}$); 5.28 (1H, d, $^2J_{\text{HH}} = 4.2$, $\text{C}=\text{CH}$); 6.25 (1H, s, NH); 6.86 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.14 (2H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.18 (2H, d, $^3J_{\text{HH}} = 7.5$, H Ar); 7.22 (1H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.28 (1H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.33 (1H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.42 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.48 (2H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.52 (2H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.63 (1H, s, H Ar); 7.68 (1H, s, H Ar); 8.12 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 14.2; 18.5; 26.8; 31.2; 38.2 (d, $J = 11.4$); 41.2 (d, $J = 156.7$); 60.3; 62.3; 77.2; 113.5; 114.3; 115.2; 116.3; 117.3; 120.7 (d, $J = 22.8$); 121.5 (d, $J = 22.8$); 123.4; 123.8; 125.3; 125.8; 126.3; 126.8; 127.6; 128.2; 128.6; 134.2; 137.6; 142.8; 151.6 (d, $J = 10.8$); 152.3 (d, $J = 10.8$); 152.6; 153.6; 154.2; 159.6; 161.2 (d, $J = 7.8$); 168.4 (d, $J = 21.7$). ^{31}P NMR spectrum, δ , ppm: 22.6. Mass spectrum, m/z (I_{rel} , %): 748 $[\text{M}]^+$ (10), 691 (64), 57 (100). Found, %: C 67.53; H 5.73; N 3.92. $\text{C}_{42}\text{H}_{41}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 67.37; H 5.52; N 3.74.

Methyl (8R,9R)-8-(dimethoxyphosphoryl)-5-(2,3,6-trimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7H-furo[2,3-*f*]chromene-9-carboxylate (6j). Yield 1.07 g (92%), yellow powder, mp 201–203°C. IR spectrum, ν , cm^{-1} : 1743, 1737, 1697, 1648, 1574, 1478, 1364, 1285. ^1H NMR spectrum, δ , ppm (J , Hz): 1.65 (3H, s, CH_3); 2.17 (3H, s, CH_3); 2.36 (3H, s, CH_3); 2.63 (3H, s, CH_3); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.83 (1H, dd, $^2J_{\text{HP}} = 19.5$, $^3J_{\text{HH}} = 11.7$, PCH); 3.87 (3H, d,

$^3J_{\text{HP}} = 11.7$, CH_3OP); 3.95 (3H, d, $^3J_{\text{HP}} = 11.7$, CH_3OP); 4.72 (1H, dd, $^3J_{\text{HH}} = 10.2$, $^3J_{\text{HP}} = 8.7$, PCCH); 4.83 (1H, d, $^2J_{\text{HH}} = 3.8$, $\text{C}=\text{CH}$); 5.16 (1H, d, $^2J_{\text{HH}} = 3.8$, $\text{C}=\text{CH}$); 6.28 (1H, s, NH); 7.02 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.24 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.45 (1H, s, H Ar); 7.58 (1H, s, H Ar); 7.95 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 18.6; 21.2; 25.4; 34.5; 42.5 (d, $J = 9.5$); 46.4 (d, $J = 144.7$); 51.3 (d, $J = 8.6$); 52.5 (d, $J = 8.6$); 53.2; 76.5; 105.3; 113.4; 114.3; 115.3; 121.6; 122.5; 122.7; 123.4; 124.4; 127.6; 133.7; 137.8; 142.5. ^{31}P NMR spectrum, δ , ppm: 19.8. Mass spectrum, m/z (I_{rel} , %): 582 $[\text{M}]^+$ (10), 551 (86), 31 (100). Found, %: C 59.92; H 5.52; N 4.97. $\text{C}_{29}\text{H}_{31}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 59.79; H 5.36; N 4.81.

Methyl (8R,9R)-8-(dimethoxyphosphoryl)-5-(3-ethyl-2,6-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-isopropenyl-7-oxo-8,9-dihydro-7H-furo[2,3-*f*]chromene-9-carboxylate (6k). Yield 1.07 g (90%), yellow powder, mp 207–209°C. IR spectrum, ν , cm^{-1} : 1742, 1736, 1698, 1637, 1589, 1482, 1387, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.27 (3H, t, $^3J_{\text{HH}} = 7.4$, CH_2CH_3); 1.75 (3H, s, CH_3); 2.16 (3H, s, CH_3); 2.35 (3H, s, CH_3); 2.76–2.85 (1H, m, CH_3CH_2); 3.13–3.27 (1H, m, CH_3CH_2); 3.78 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.83 (1H, dd, $^2J_{\text{HP}} = 19.7$, $^3J_{\text{HH}} = 11.5$, PCH); 3.92 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.96 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.75 (1H, dd, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{HP}} = 10.3$, PCCH); 4.85 (1H, d, $^2J_{\text{HH}} = 4.7$, $\text{C}=\text{CH}$); 5.26 (1H, d, $^2J_{\text{HH}} = 4.7$, $\text{C}=\text{CH}$); 6.22 (1H, s, NH); 7.12 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.28 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.49 (1H, s, H Ar); 7.56 (1H, s, H Ar); 7.93 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 14.2; 18.6; 22.4; 25.6; 40.5; 42.7 (d, $^2J_{\text{PC}} = 9.8$); 45.9 (d, $^1J_{\text{PC}} = 145.3$); 51.4 (d, $J = 9.3$); 52.6 (d, $J = 9.3$); 53.5; 76.7; 106.3; 113.7; 114.2; 114.7; 121.9; 122.6; 123.2; 123.8; 124.5; 127.5; 131.6; 137.4; 142.3; 151.4; 152.2; 154.7; 160.7; 161.6 (d, $J = 6.8$); 168.4 (d, $J = 22.5$). ^{31}P NMR spectrum, δ , ppm: 21.2. Mass spectrum, m/z (I_{rel} , %): 596 $[\text{M}]^+$ (15), 565 (84), 31 (100). Found, %: C 60.52; H 5.73; N 4.85. $\text{C}_{30}\text{H}_{33}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 60.40; H 5.58; N 4.70.

Methyl (8R,9R)-5-[3-(*tert*-butyl)-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl]-8-(dimethoxyphosphoryl)-2-isopropenyl-7-oxo-8,9-dihydro-7H-furo[2,3-*f*]chromene-9-carboxylate (6l). Yield 1.11 g (85%), yellow powder, mp 222–224°C. IR spectrum, ν , cm^{-1} : 1739, 1735, 1685, 1656, 1578, 1486, 1383, 1292. ^1H NMR spectrum, δ , ppm (J , Hz): 1.18 (9H, s, $\text{C}(\text{CH}_3)_3$); 1.65 (3H, s, CH_3); 2.23 (3H, s, CH_3); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.87 (1H, dd, $^2J_{\text{HP}} = 21.2$, $^3J_{\text{HH}} = 12.3$, PCH); 3.92 (3H, d, $^3J_{\text{HP}} = 12.3$, CH_3OP); 3.96 (3H, d, $^3J_{\text{HP}} = 12.3$, CH_3OP); 4.75 (1H, d, $^2J_{\text{HH}} = 5.2$, $\text{C}=\text{CH}$); 4.88 (1H, dd, $^3J_{\text{HH}} = 11.7$, $^3J_{\text{HP}} = 9.5$, PCCH); 5.18 (1H, d, $^2J_{\text{HH}} = 5.2$, $\text{C}=\text{CH}$); 6.27 (1H, s, NH); 7.15 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.32 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.46 (1H, s, H Ar); 7.58 (1H, s, H Ar); 8.37 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 18.5; 27.6; 31.6; 43.2 (d, $J = 10.5$); 47.6 (d, $J = 148.4$); 51.6 (d, $J = 9.2$); 52.4 (d, $J = 9.2$); 53.2; 62.5; 77.8; 113.6; 114.5; 114.9; 115.5; 116.7; 123.4; 123.9; 124.6; 127.8; 134.6; 137.5; 138.8; 142.3; 152.7; 153.2; 155.3; 161.2; 161.7 (d, $J = 6.7$); 169.5 (d, $J = 21.4$). ^{31}P NMR spectrum, δ , ppm: 22.3. Mass spectrum, m/z (I_{rel} , %): 655 $[\text{M}]^+$ (10), 598 (78), 31 (100). Found, %: C 56.92; H 5.43; N 6.67. $\text{C}_{31}\text{H}_{34}\text{N}_3\text{O}_{11}\text{P}$. Calculated, %: C 56.79; H 5.23; N 6.41.

Methyl (8*R*,9*R*)-5-(6-chloro-3-isopropyl-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-8-(dimethoxyphosphoryl)-2-isopropenyl-7-oxo-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6*m*). Yield 1.09 g (87%), yellow powder, mp 232–235°C. IR spectrum, ν , cm^{-1} : 1739, 1735, 1692, 1663, 1585, 1486, 1378, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.16 (6H, d, $^3J_{\text{HH}} = 6.8$, $\text{C}(\text{CH}_3)_2$); 1.75 (3H, s, CH_3); 2.18 (3H, s, CH_3); 3.73 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.75–3.86 (2H, m, 2 CH); 3.92 (3H, d, $^3J_{\text{HP}} = 11.8$, CH_3OP); 3.97 (3H, d, $^3J_{\text{HP}} = 11.8$, CH_3OP); 4.76 (1H, d, $^2J_{\text{HH}} = 4.9$, $\text{C}=\text{CH}$); 4.86 (1H, dd, $^3J_{\text{HH}} = 11.3$, $^3J_{\text{HP}} = 10.5$, PCCH); 5.12 (1H, d, $^2J_{\text{HH}} = 4.9$, $\text{C}=\text{CH}$); 6.22 (1H, s, NH); 7.16 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.37 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.52 (1H, s, H Ar); 7.67 (1H, s, H Ar); 8.23 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 18.6; 22.5; 26.5; 42.7 (d, $J = 10.7$); 43.7; 47.8 (d, $J = 148.5$); 51.4 (d, $J = 10.3$); 52.7 (d, $J = 10.3$); 53.5; 76.4; 105.8; 113.6; 114.7; 115.2; 121.5; 122.4; 122.7; 126.2; 127.6; 128.2; 133.7; 137.5; 142.6; 152.3; 153.4; 154.6; 161.7; 162.5 (d, $J = 6.9$); 172.3 (d, $J = 22.5$). ^{31}P NMR spectrum, δ , ppm: 22.8. Mass spectrum, m/z (I_{rel} , %): 631 $[\text{M}]^+$ (15), 600 (68), 31 (100). Found, %: C 57.25; H 5.27; N 4.62. $\text{C}_{30}\text{H}_{32}\text{ClN}_2\text{O}_9\text{P}$. Calculated, %: C 57.10; H 5.11; N 4.44.

Methyl (8*R*,9*R*)-8-(diphenoxyphosphoryl)-2-isopropenyl-7-oxo-5-(2,3,6-trimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-8,9-dihydro-7*H*-furo[2,3-*f*]chromene-9-carboxylate (6*n*). Yield 1.23 g (87%), pale-yellow powder, mp 218–220°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1695, 1673, 1587, 1485, 1389, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.67 (3H, s, CH_3); 2.16 (3H, s, CH_3); 2.27 (3H, s, CH_3); 2.52 (3H, s, CH_3); 3.67 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 4.28 (1H, dd, $^2J_{\text{HP}} = 18.7$, $^3J_{\text{HH}} = 11.5$, PCH); 4.87 (1H, dd, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HP}} = 10.5$, PCCH); 4.95 (1H, d, $^2J_{\text{HH}} = 5.3$, $\text{C}=\text{CH}$); 5.25 (1H, d, $^2J_{\text{HH}} = 5.3$, $\text{C}=\text{CH}$); 6.37 (1H, s, NH); 6.95 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.15 (2H, d, $^3J_{\text{HH}} = 7.5$, H Ar); 7.18 (2H, d, $^3J_{\text{HH}} = 7.5$, H Ar); 7.25 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.32 (1H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.38 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.45 (2H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.52 (2H, t, $^3J_{\text{HH}} = 7.5$, H Ar); 7.58 (1H, s, H Ar); 7.63 (1H, s, H Ar); 8.12 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 18.6; 22.4; 24.7; 34.6; 38.2 (d, $J = 9.8$); 40.4 (d, $J = 158.5$); 51.8; 78.2; 107.6; 113.5; 114.3; 115.6; 121.2 (d, $J = 22.8$); 121.7 (2CH, d, $^3J_{\text{PC}} = 22.8$); 122.7 (C); 123.2 (CH); 123.6 (C); 124.2 (C); 125.4 (2CH); 126.4 (CH); 127.5 (CH); 128.5 (2CH); 129.2 (2CH); 133.6 (CH); 137.8 (C); 142.3 (C); 151.7 (d, $^2J_{\text{PC}} = 10.5$); 152.3 (d, $^2J_{\text{PC}} = 10.7$); 152.6 (C); 153.8 (C); 154.7 (C); 159.6 (C=O); 161.2 (d, $^2J_{\text{PC}} = 7.5$, C=O); 166.3 (d, $^3J_{\text{PC}} = 22.5$, C=O). ^{31}P NMR spectrum, δ , ppm: 21.3. Mass spectrum, m/z (I_{rel} , %): 706 $[\text{M}]^+$ (10), 675 (74), 31 (100). Found, %: C 66.42; H 5.16; N 4.23. $\text{C}_{39}\text{H}_{35}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 66.28; H 4.99; N 3.96.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(2,3-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-2-oxo-4-chromene carboxylate (16*a*). Yield 0.95 g (97%), white powder, mp 115–117°C. IR spectrum, ν , cm^{-1} : 1743, 1735, 1687, 1637, 1587, 1465, 1378, 1286. ^1H NMR spectrum, δ , ppm (J , Hz): 1.65 (3H, s, CH_3); 2.58 (3H, s, CH_3); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.83 (1H, dd, $^2J_{\text{HP}} = 18.7$, $^3J_{\text{HH}} = 11.5$, PCH); 3.87 (3H, d, $^3J_{\text{HP}} = 10.8$, CH_3OP); 3.93 (3H, d, $^3J_{\text{HP}} = 10.8$, CH_3OP); 4.72 (1H, dd, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HP}} = 9.2$,

PCCH); 6.18 (1H, s, NH); 6.95 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.15 (1H, t, $^3J_{\text{HH}} = 7.8$, H Ar); 7.18 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.23 (1H, t, $^3J_{\text{HH}} = 7.8$, H Ar); 7.34 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.62 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.93 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 25.3; 34.2; 42.3 (d, $J = 9.3$); 46.3 (d, $J = 143.2$); 51.2 (d, $J = 8.7$); 52.4 (d, $J = 8.7$); 52.8; 76.4; 110.3; 114.8; 121.6; 123.4 (d, $J = 5.6$); 124.3; 125.2; 126.4; 127.4; 128.3; 133.6; 142.3; 152.3; 160.3; 161.3 (d, $J = 6.8$); 167.5 (d, $J = 22.5$). ^{31}P NMR spectrum, δ , ppm: 20.3. Mass spectrum, m/z (I_{rel} , %): 488 $[\text{M}]^+$ (15), 457 (68), 31 (100). Found, %: C 56.72; H 5.32; N 5.92. $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_8\text{P}$. Calculated, %: C 56.56; H 5.16; N 5.74.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(3-ethyl-2-methyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-6-methoxy-2-oxo-4-chromene carboxylate (16*b*). Yield 1.01 g (95%), white powder, mp 123–125°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1695, 1654, 1593, 1487, 1395, 1286. ^1H NMR spectrum, δ , ppm (J , Hz): 1.27 (3H, t, $^3J_{\text{HH}} = 7.3$, CH_3); 2.17 (3H, s, CH_3); 2.76–2.84 (1H, m, CH_2CH_3); 3.15–3.25 (1H, m, CH_2CH_3); 3.75 (3H, s, CH_3O); 3.78 (3H, s, CH_3O); 3.83 (1H, dd, $^2J_{\text{HP}} = 19.7$, $^3J_{\text{HH}} = 11.6$, PCH); 3.92 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.96 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.75 (1H, dd, $^3J_{\text{HH}} = 11.6$, $^3J_{\text{HP}} = 10.4$, PCCH); 6.22 (1H, s, NH); 6.75 (1H, s, H Ar); 7.05 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.08 (1H, s, H Ar); 7.23 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.32 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.85 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 13.8; 24.3; 41.3; 42.7 (d, $J = 9.5$); 46.2 (d, $J = 146.3$); 51.5 (d, $J = 9.7$); 52.7 (d, $J = 9.7$); 53.4; 55.6; 77.5; 110.3; 112.2; 114.2; 115.2; 122.2; 122.7; 123.4; 125.6; 128.4; 142.5; 143.4; 155.6; 161.2; 162.3 (d, $J = 7.5$); 168.5 (d, $J = 21.8$). ^{31}P NMR spectrum, δ , ppm: 21.2. Mass spectrum, m/z (I_{rel} , %): 582 $[\text{M}]^+$ (15), 551 (86), 31 (100). Found, %: C 56.52; H 5.63; N 5.42. $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 56.39; H 5.49; N 5.26.

Methyl (3*R*,4*R*)-8-[3-(*tert*-butyl)-2,6-dimethyl-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl]-3-(dimethoxyphosphoryl)-6-methoxy-2-oxo-4-chromene carboxylate (16*c*). Yield 1.09 g (95%), white powder, mp 127–129°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1687, 1653, 1584, 1483, 1378, 1262. ^1H NMR spectrum, δ , ppm (J , Hz): 1.18 (9H, s, $\text{C}(\text{CH}_3)_3$); 1.75 (3H, s, CH_3); 2.36 (3H, s, CH_3); 3.75 (3H, s, CH_3O); 3.83 (1H, dd, $^2J_{\text{HP}} = 20.6$, $^3J_{\text{HH}} = 11.8$, PCH); 3.87 (3H, s, CH_3O); 3.92 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.97 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.86 (1H, dd, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HP}} = 9.5$, PCCH); 6.27 (1H, s, NH); 6.95 (1H, s, H Ar); 7.06 (1H, s, H Ar); 7.12 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.27 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 8.14 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 21.3; 27.6; 31.5; 42.8 (d, $J = 10.2$); 47.5 (d, $J = 147.4$); 51.6 (d, $J = 9.7$); 52.4 (d, $J = 9.7$); 53.6; 55.7; 62.5; 81.3; 106.3; 111.4; 113.3; 122.4; 123.2; 124.8; 125.4; 127.2; 129.4; 143.2; 145.3; 158.3; 161.6 (d, $J = 6.7$); 162.3; 168.7 (d, $J = 21.5$). ^{31}P NMR spectrum, δ , ppm: 21.7. Mass spectrum, m/z (I_{rel} , %): 574 $[\text{M}]^+$ (15), 517 (64), 57 (100), 31 (100). Found, %: C 58.52; H 6.32; N 4.97. $\text{C}_{28}\text{H}_{35}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 58.53; H 6.14; N 4.88.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(3-isopropyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydro-2-quinazolinyl)-5-methyl-2-oxo-4-chromene carboxylate (16*d*). Yield 0.98 g (90%), pale-yellow powder, mp 147–149°C. IR spectrum, ν , cm^{-1} : 1740, 1738, 1692, 1667, 1587, 1485,

1384, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.15 (6H, d, $^3J_{\text{HH}} = 6.7$, $\text{C}(\text{CH}_3)_2$); 1.75 (3H, s, CH_3); 2.23 (3H, s, CH_3); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.75–3.86 (2H, m, $\text{CH}(\text{CH}_3)_2$, PCH); 3.83 (3H, d, $^3J_{\text{HP}} = 11.8$, CH_3OP); 3.89 (3H, d, $^3J_{\text{HP}} = 12.2$, CH_3OP); 4.85 (1H, dd, $^3J_{\text{HH}} = 12.2$, $^3J_{\text{HP}} = 10.5$, PCCH); 6.25 (1H, s, NH); 7.12 (1H, d, $^3J_{\text{HH}} = 7.5$, H Ar); 7.27 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.63 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 8.16 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 8.68 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 21.4; 22.4; 26.4; 42.5 (d, $J = 10.6$); 43.7; 47.7 (d, $J = 147.2$); 51.8 (d, $J = 10.2$); 52.6 (d, $J = 10.2$); 53.4; 78.3; 112.2; 112.6; 121.3; 124.2; 127.2; 129.7; 130.2; 131.5; 132.3; 138.3; 146.4; 148.6; 161.4; 162.5 (d, $J = 6.7$); 172.6 (d, $J = 22.3$). ^{31}P NMR spectrum, δ , ppm: 23.4. Mass spectrum, m/z (I_{rel} , %): 575 $[\text{M}]^+$ (15), 544 (68), 31 (100). Found, %: C 54.42; H 5.43; N 7.45. $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_{10}\text{P}$. Calculated, %: C 54.26; H 5.25; N 7.30.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl)-2-oxo-4-chromene carboxylate (16e). Yield 0.92 g (97%), white powder, mp 112–114°C. IR spectrum, ν , cm^{-1} : 1740, 1739, 1685, 1638, 1575, 1478, 1386, 1274. ^1H NMR spectrum, δ , ppm (J , Hz): 3.48 (3H, s, NCH_3); 3.75 (3H, s, $\text{C}(\text{O})\text{OCH}_3$); 3.83 (1H, dd, $^2J_{\text{HP}} = 18.7$, $^3J_{\text{HH}} = 11.4$, PCH); 3.89 (3H, d, $^3J_{\text{HP}} = 11.6$, CH_3OP); 3.95 (3H, d, $^3J_{\text{HP}} = 11.6$, CH_3OP); 4.74 (1H, dd, $^3J_{\text{HH}} = 11.4$, $^3J_{\text{HP}} = 8.9$, PCCH); 7.34 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.48 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.56 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.68 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.74 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.85 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 8.22 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 32.3; 43.4 (d, $J = 144.7$); 46.5 (d, $J = 10.8$); 51.3 (d, $J = 8.9$); 52.5 (d, $J = 8.9$); 53.2; 121.3; 122.4; 125.3; 126.2; 126.8; 127.5; 128.3; 129.2; 130.2; 135.6; 146.2; 156.2; 160.5; 161.6 (d, $J = 6.7$); 165.2; 168.2 (d, $J = 22.5$). ^{31}P NMR spectrum, δ , ppm: 21.2. Mass spectrum, m/z (I_{rel} , %): 472 $[\text{M}]^+$ (15), 441 (86), 31 (100). Found, %: C 56.12; H 4.62; N 6.16. $\text{C}_{22}\text{H}_{21}\text{N}_2\text{O}_8\text{P}$. Calculated, %: C 55.94; H 4.48; N 5.93.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(3-ethyl-2-methyl-4-oxo-3,4-dihydro-2-quinazolinyl)-6-methoxy-2-oxo-4-chromene carboxylate (16f). Yield 0.98 g (95%), white powder, mp 123–125°C. IR spectrum, ν , cm^{-1} : 1742, 1738, 1689, 1678, 1565, 1478, 1376, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.27 (3H, t, $^3J_{\text{HH}} = 7.3$, $\text{CH}_2\text{CH}_3\text{N}$); 3.34 (2H, q, $^3J_{\text{HH}} = 7.3$, $\text{CH}_2\text{CH}_3\text{N}$); 3.75 (3H, s, CH_3O); 3.83 (3H, s, CH_3O); 3.88 (1H, dd, $^2J_{\text{HP}} = 18.7$, $^3J_{\text{HH}} = 11.5$, PCH); 3.92 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.97 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.76 (1H, dd, $^3J_{\text{HH}} = 11.5$, $^3J_{\text{HP}} = 10.5$, PCCH); 6.95 (1H, s, H Ar); 7.12 (1H, s, H Ar); 7.45 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.65 (1H, t, $^3J_{\text{HH}} = 7.6$, H Ar); 7.78 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 8.12 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 13.8; 38.2; 43.4 (d, $J = 9.7$); 46.2 (d, $J = 146.3$); 51.3 (d, $J = 9.7$); 52.6 (d, $J = 9.7$); 53.3; 55.8; 109.2; 114.3; 121.3; 122.4; 126.2; 127.4; 128.6; 134.2; 145.2; 149.5; 157.2; 160.7; 162.3 (d, $J = 7.5$); 165.6; 168.4 (d, $J = 21.7$). ^{31}P NMR spectrum, δ , ppm: 21.6. Mass spectrum, m/z (I_{rel} , %): 516 $[\text{M}]^+$ (10), 485 (64), 31 (100). Found, %: C 55.97; H 4.96; N 5.63. $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 55.82; H 4.88; N 5.42.

Methyl (3*R*,4*R*)-8-[3-(*tert*-butyl)-6-methyl-4-oxo-3,4-dihydro-2-quinazolinyl]-3-(dimethoxyphosphoryl)-6-methoxy-2-oxo-4-chromene carboxylate (16g). Yield 1.06 g

(95%), white powder, mp 136–138°C. IR spectrum, ν , cm^{-1} : 1742, 1739, 1688, 1674, 1587, 1469, 1372, 1295. ^1H NMR spectrum, δ , ppm (J , Hz): 1.46 (9H, s, $\text{C}(\text{CH}_3)_3$); 2.35 (3H, s, CH_3); 3.75 (3H, s, CH_3O); 3.78 (3H, s, CH_3O); 3.82 (1H, dd, $^2J_{\text{HP}} = 19.8$, $^3J_{\text{HH}} = 11.5$, PCH); 3.88 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 3.95 (3H, d, $^3J_{\text{HP}} = 11.5$, CH_3OP); 4.87 (1H, dd, $^3J_{\text{HH}} = 11.7$, $^3J_{\text{HP}} = 9.5$, PCCH); 6.85 (1H, s, H Ar); 7.05 (1H, s, H Ar); 7.56 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.82 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.97 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 21.3; 30.7; 42.8 (d, $J = 10.6$); 48.2 (d, $J = 147.5$); 51.7 (d, $J = 9.8$); 52.4 (d, $J = 9.8$); 52.8; 55.7; 61.3; 111.3; 114.5; 121.3; 122.8; 124.3; 125.6; 128.4; 131.4; 137.2; 143.4; 151.2; 157.4; 160.2 (d, $J = 6.3$); 161.4; 164.3; 167.4 (d, $J = 21.5$). ^{31}P NMR spectrum, δ , ppm: 22.4. Mass spectrum, m/z (I_{rel} , %): 558 $[\text{M}]^+$ (10), 527 (78), 31 (100). Found, %: C 58.24; H 5.75; N 5.18. $\text{C}_{27}\text{H}_{31}\text{N}_2\text{O}_9\text{P}$. Calculated, %: C 58.06; H 5.59; N 5.02.

Methyl (3*R*,4*R*)-3-(dimethoxyphosphoryl)-8-(3-isopropyl-6-nitro-4-oxo-3,4-dihydro-2-quinazolinyl)-5-methoxy-2-oxo-4-chromene carboxylate (16h). Yield 1.04 g (90%), pale-yellow powder, mp 145–147°C. IR spectrum, ν , cm^{-1} : 1743, 1739, 1698, 1678, 1582, 1487, 1363, 1258. ^1H NMR spectrum, δ , ppm (J , Hz): 1.28 (6H, d, $^3J_{\text{HH}} = 6.9$, $\text{CH}(\text{CH}_3)_2$); 3.68 (3H, s, CH_3O); 3.74 (1H, dd, $^2J_{\text{HP}} = 19.5$, $^3J_{\text{HH}} = 11.8$, PCH); 3.80 (3H, s, CH_3O); 3.85 (3H, d, $^3J_{\text{HP}} = 11.8$, CH_3OP); 3.93 (3H, d, $^3J_{\text{HP}} = 11.8$, CH_3OP); 4.93 (1H, dd, $^3J_{\text{HH}} = 11.8$, $^3J_{\text{HP}} = 10.8$, PCCH); 5.65–5.72 (1H, m, NCH); 6.68 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.57 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 7.63 (1H, d, $^3J_{\text{HH}} = 7.6$, H Ar); 7.87 (1H, d, $^3J_{\text{HH}} = 7.8$, H Ar); 8.47 (1H, s, H Ar). ^{13}C NMR spectrum, δ , ppm (J , Hz): 21.8; 42.5 (d, $J = 10.8$); 46.8; 47.9 (d, $J = 147.5$); 51.3 (d, $J = 10.6$); 52.2 (d, $J = 10.6$); 52.8; 55.4; 112.4; 113.8; 120.4; 122.3; 123.4; 125.2; 128.2; 130.4; 147.2; 149.3; 153.2; 154.8; 160.2; 161.8 (d, $J = 6.3$); 163.8; 168.3 (d, $J = 21.7$). ^{31}P NMR spectrum, δ , ppm: 22.8. Mass spectrum, m/z (I_{rel} , %): 575 $[\text{M}]^+$ (10), 544 (68), 31 (100). Found, %: C 52.28; H 4.72; N 7.45. $\text{C}_{25}\text{H}_{26}\text{N}_3\text{O}_{11}\text{P}$. Calculated, %: C 52.18; H 4.55; N 7.30.

Supplementary information file containing ^1H and ^{13}C NMR spectra of selected compounds is available at the journal website at <http://link.springer.com/journal/10593>.

We gratefully acknowledge for spiritual support from Islamic Azad University of Qaemshahr Branch.

References

- (a) Kantam, M. L.; Rajasekhar, Ch. V.; Gopikrishna, G.; Reddy, K. R.; Choudary, B. M. *Tetrahedron Lett.* **2006**, 47, 5965. (b) Liu, Y.-Q.; Li, L.-H.; Yang, L.; Li, H.-Y. *Chem. Pap.* **2010**, 64, 533.
- Kaur, N. *Synth. Commun.* **2018**, 48, 1235.
- Mohammadi Ziarani, Gh.; kheilkordi, Z.; Gholamzadeh *Mol. Diversity* **2020**, 24, 771.
- (a) Mečiarová, M.; Poláček, V.; Toma, Š. *Chem. Pap.* **2002**, 56, 208. (b) Meciarova, M.; Toma, S.; Babiak, P. *Chem. Pap.* **2004**, 58, 104.
- Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, A. *Catal. Commun.* **2008**, 9, 416.
- Meciarova, M.; Toma, S.; Lucche, J. L. *Ultrason. Sonochem.* **2001**, 8, 119.

7. Vinatoru, M.; Bartha, E.; Badea, F.; Luche, J. L. *Ultrason. Sonochem.* **1998**, *5*, 27.
8. Ando, T.; Kimura, T.; Fujita, M.; Levêque, J.-M.; Luche, J.-L. *Tetrahedron Lett.* **2001**, *42*, 6865.
9. Cabello, N.; Cintas, P.; Luche, J.-L. *Ultrason. Sonochem.* **2003**, *10*, 25.
10. Kumar, V.; Sharma, A.; Sharma, M.; Sharma, U. K.; Sinha, A. K. *Tetrahedron* **2007**, *63*, 9718.
11. Sinha, A. K.; Sharma, A.; Joshi, B. P. *Tetrahedron* **2007**, *63*, 960.
12. Rostami-Charati, F.; Hossaini, Z. S. *Synlett* **2012**, 2397.
13. (a) Hailes, H. C. *Org. Process Res. Dev.* **2007**, *11*, 114. (b) Jiang, B.; Cao, L.-J.; Tu, S.-J.; Zheng, W.-R.; Yu, H.-Z. *J. Comb. Chem.* **2009**, *11*, 612. (c) Tu, S.-J.; Zhang, X.-H.; Han, Z.-G.; Cao, X.-D.; Wu, S.-S.; Yan, S.; Hao, W.-J.; Zhang, G.; Ma, N. *J. Comb. Chem.* **2009**, *11*, 428. (d) Wu, H.; Lin, W.; Wan, Y.; Xin, H.-q.; Shi, D.-q.; Shi, Y.-h.; Yuan, R.; Bo, R.-c.; Yin, W. *J. Comb. Chem.* **2010**, *12*, 31. (e) Erdmenger, T.; Guerrero-Sanchez, C.; Vitz, J.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.* **2010**, *39*, 3317.
14. (a) Imamoto, T. *Handbook of Organophosphorus Chemistry*; Engel, R., Ed.; Marcel Dekker: New York, 1992, Chap. 1, p. 1. (b) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley-Interscience: New York, 2000. (c) Sasaki, M. *Chirality in Agrochemicals*; Kurihara, N., Miyamoto, J., Eds.; Wiley & Sons: Chichester, 1998, p. 85.
15. (a) Baumgartner, T.; Réau, R. *Chem. Rev.* **2006**, *106*, 4681. (b) Engel, R. *Chem. Rev.* **1977**, *77*, 349. (c) Witt, M.; Roesky, H. W. *Chem. Rev.* **1994**, *94*, 1163. (d) Arduengo, A. J., III; Stewart, C. A. *Chem. Rev.* **1994**, *94*, 1215. (e) Cristau, H.-J. *Chem. Rev.* **1994**, *94*, 1299. (f) Gorenstein, D. G. *Chem. Rev.* **1994**, *94*, 1315. (g) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.
16. (a) Kim, Y.-C.; Brown, S. G.; Harden, T. K.; Boyer, J. L.; Dubyak, G.; King, B. F.; Burnstock, G.; Jacobson, K. A. *J. Med. Chem.* **2001**, *44*, 340. (b) Kumar, T. S.; Zhou, S.-Y.; Joshi, B. V.; Balasubramanian, R.; Yang, T.; Liang, B. T.; Jacobson, K. A. *J. Med. Chem.* **2010**, *53*, 2562. (c) Shie, J.-J.; Fang, J.-M.; Wang, S.-Y.; Tsai, K.-C.; Cheng, Y.-S. E.; Yang, A.-S.; Hsiao, S.-C.; Su, C.-Y.; Wong, C.-H. *J. Am. Chem. Soc.* **2007**, *129*, 11892.
17. (a) Kukhar, V. P.; Hudson, H. R. *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity*; Wiley & Sons: Chichester, 2000. (b) Sawa, M.; Tsukamoto, T.; Kiyoi, T.; Kurokawa, K.; Nakajima, F.; Nakada, Y.; Yokota, K.; Inoue, Y.; Kondo, H.; Yoshino, K. *J. Med. Chem.* **2002**, *45*, 930. (c) Camp, N. P.; Perry, D. A.; Kinchington, D.; Hawkins, P. C. D.; Hitchcock, P. B.; Gani, D. *Bioorg. Med. Chem.* **1995**, *3*, 297. (d) Zhou, Y.; Yin, S.; Gao, Y.; Zhao, Y.; Goto, M.; Han, L.-B. *Angew. Chem., Int. Ed.* **2010**, *49*, 6852.
18. Allenberger, F.; Klare, L. *J. Antimicrob. Chemother.* **1999**, *43*, 211.
19. Allen, J. G.; Atherton, F. R.; Hall, M. J.; Hassall, C. H.; Holmes, S. W.; Lambert, R. W.; Nisbet, L. J.; Ringrose, P. S. *Nature* **1978**, *272*, 56.
20. Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E. *Tetrahedron Lett.* **1990**, *31*, 5587.
21. Bader, A. *Aldrichimica Acta* **1988**, *21*, 15.
22. Horsman, G. P.; Zechel, D. L. *Chem. Rev.* **2017**, *117*, 5704.
23. Mikołajczyk, M. *Pure Appl. Chem.* **2019**, *91*, 811.
24. Kosolapoff, G. M.; Maier, L. *Organic Phosphorus Compounds*; Wiley-Interscience, 1972.
25. Hudson, H. R. In *The Chemistry of Organophosphorus Compounds: Primary Secondary and Tertiary Phosphines and Heterocyclic Organophosphorus(III) Compounds*; Hantely, F. R.; Patai, S., Eds.; Wiley: New York, 1990, p. 386.
26. Engel, R.; Cohen, J. I. *Synthesis of Carbon-Phosphorus Bonds*; CRC Press: Boca Raton, 1998.
27. (a) Yavari, I.; Hossaini, Z.; Alizadeh, A. *Monatsh. Chem.* **2006**, *137*, 1083. (b) Alizadeh, A.; Yavari, I. *Mendeleev Commun.* **2005**, *14*, 154. (c) Yavari, I.; Alizadeh, A. *Synthesis* **2004**, 237. (d) Yavari, I.; Alizadeh, A.; Anary-Abbasinejad, M. *Tetrahedron. Lett.* **2003**, *44*, 2877. (e) Yavari, I.; Anary-Abbasinejad, M.; Hossaini, Z. *Org. Biomol. Chem.* **2003**, *1*, 560.
28. Yavari, I.; Hossaini, Z.; Karimi, E. *Monatsh. Chem.* **2007**, *138*, 1267.
29. Anary-Abbasinejad, M.; Hassanabadi, A.; Mazraeh-Seffid, M. *J. Chem. Res.* **2007**, 708.
30. Hallajian, S.; Alipour, S.; Foroughifar, N.; Khalilzadeh, M. A. *Orient. J. Chem.* **2014**, *30*, 1311.
31. Labaudiniere, L.; Burgada, R. *Tetrahedron* **1986**, *42*, 3521.
32. Bartoli, J.; Turmo, E.; Algueró, M.; Boncompagni, E.; Vericat, M. L.; Conte, L.; Ramis, J.; Merlos, M.; Gracia-Rafanell, J.; Forn, J. *J. Med. Chem.* **1998**, *41*, 1869.
33. Zhu, S.; Wang, J.; Chandrashekar, G.; Smith, E.; Liu, X.; Zhang, Y. *Eur. J. Med. Chem.* **2010**, *45*, 3864.
34. Al-Rashood, S. T.; Hassan, G. S.; El-Messery, S. M.; Nagi, M. N.; Habib, E.-S. E.; Al-Omary, F. A. M.; El-Subbagh, H. I. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 4557.
35. Hour, M.-J.; Huang, L.-J.; Kuo, S.-C.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **2000**, *43*, 4479.
36. (a) Su, W.; Yang, B. *Aust. J. Chem.* **2002**, *55*, 695. (b) Shi, D.; Rong, L.; Wang, J.; Zhuang, Q.; Wang, X.; Hu, H. *Tetrahedron Lett.* **2003**, *44*, 3199.
37. Khurana, J. M.; Kukreja, G. *J. Heterocycl. Chem.* **2003**, *40*, 677.
38. Yale, H. L. *J. Heterocycl. Chem.* **1977**, *14*, 1357.
39. Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webster, W. *J. Org. Chem.* **1969**, *34*, 887.
40. Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. *Synlett* **2005**, 1155.
41. Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozhegary, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123.
42. Khaleghi, F.; Bin Din, L.; Rostami Charati, F.; Yaacob, W. A.; Khalilzadeh, M. A.; Skelton, B.; Makha, M. *Phytochem. Lett.* **2011**, *4*, 254.
43. Rostami-Charati, F.; Hossaini, Z. *Synlett* **2012**, 2397.
44. Dastoorani, P.; Maghsoodlou, M. T.; Khalilzadeh, M. A.; García-Granda, S.; Torre-Fernández, L.; Sarina, E. *Heteroat. Chem.* **2016**, 27, 102.
45. (a) Engle, R. *Synthesis of Carbon-Phosphorus Bond*; CRC Press: Boca Raton, 1988. (b) *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: New York, 1977.
46. *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: New York, 1979.