Synthesis of chalcones derived from (+)- and (−)-usnic acids*

D. N. Sokolov, O. A. Luzina, M. P. Polovinka, N. F. Salakhutdinov, and G. A. Tolstikov*

N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry,
Siberian Branch of the Russian Academy of Sciences,
9 prosp. Akad. Lavrent´eva, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383) 330 8850. E-mail: dsokolov@nioch.nsc.ru

A number of chalcones with the (+)- and (−)-usnic acid moieties were synthesized by the following sequence: the reaction of these acids with phenylhydrazine, reduction of the C(1)=O group with sodium borohydride, O-methylation of the intermediate compounds with diazomethane, and subsequent condensation with substituted benzaldehydes at the acetyl group.

Key words: usnic acid, Claisen—Schmidt condensation, flavonoids, diazomethane, chalcones.

Chalcone (1,3-diphenylprop-2-en-1-one) derivatives is a wide group of naturally occurring open-chain flavonoids. They possess antibacterial, antifungal, anticancer, antiinflammatory activities, and a number of other valuable biological properties.[1] Chalcones are commonly obtained by condensation of benzaldehydes and acetophenones.[2,3]

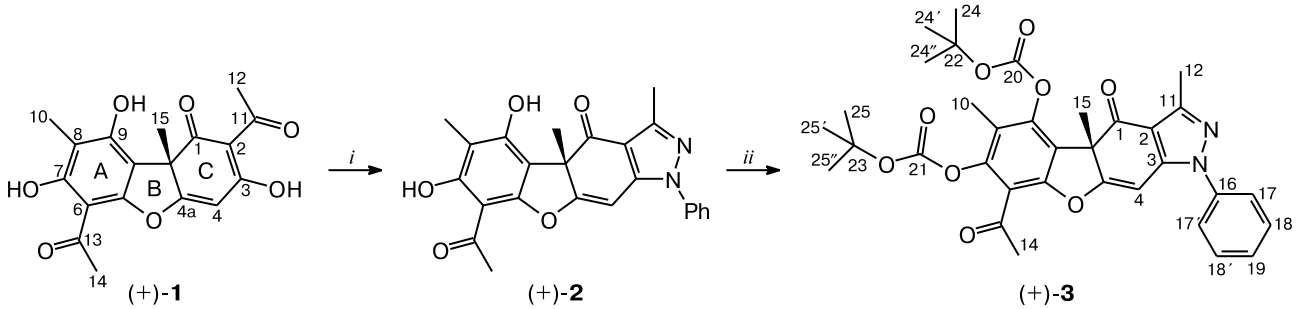
Introduction of a fragment with the native biological activity into the chalcone structure can lead to its enhancement and/or preparation of compounds with new biological properties. The secondary metabolite of the lichen series, usnic acid (**1**), possessing antiviral, antibiotic, analgesic,[4] antituberculosis,[5] and insecticide activity, seems a promising compound.[6] Some lichen species are selective producents of levo- and dextrorotating enantiomers of usnic acid with high optical purity, that broadens synthetic potential and further application of the products of its chemical modification.

The structure of usnic acid (**1**) contains an acetophenone fragment, which seems promising for the construction of chalcones. At the same time, no data on the transformation of usnic acid to the corresponding chalcones are currently known.

We have attempted to involve acid **1** into condensation with a number of benzaldehydes under conditions commonly used for the preparation of chalcones. However, the use of H_2SO_4 or K_2CO_3 as catalysts did not lead to the expected products, whereas application of strong alkali (KOH) caused destruction of the starting acid. Destruction of compound (+)-**1** upon the action of an alkali is described in the work,[7] which showed that the initial cleavage occurs in the ring C. It seems that for the base-catalyzed conversion of compound (+)-**1** to be successful, an introduction of protecting groups to the corresponding positions of the molecule is required.

We carried out chemical modifications of usnic acid (**1**) directed on the increase in its stability in basic medium. The reaction with phenylhydrazine led to pyrazole derivative (+)-**2** (Scheme 1). Unfortunately, attempted

Scheme 1



Reaction conditions: *i*. $PhNHNH_2$; *ii*. Boc_2O, DMAP.

* Dedicated to Academician of the Russian Academy of Sciences O. M. Nefedov on the occasion of his 80th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2359—2364, November, 2011.

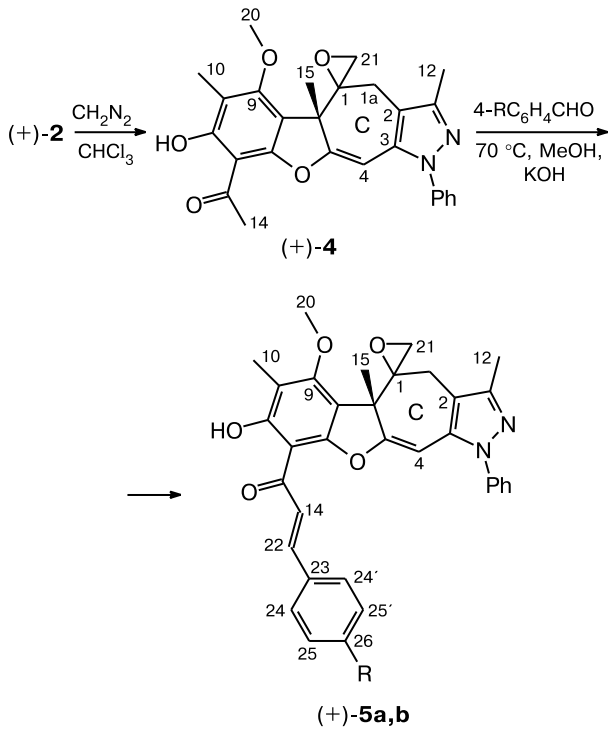
1066-5285/11/6011-2406

involvement of this compound into the base-catalyzed condensation with benzaldehyde led to the destruction of the substrate, whereas under conditions of acid catalysis, the starting reactants remained unchanged.

To increase resistance of compound (+)-**2** to the basic medium, we attempted selection of protecting groups for the phenol hydroxyls. These attempts showed that the reactants and reaction conditions tried for the protection of the phenol hydroxy groups in compound (+)-**2** (MeI, Me_2SO_4, DHP) turned out to be inefficient: either the yields of the products were low, or the reaction did not take place at all. Usnic acid is known[8,9] to react with carboxylic anhydrides with the formation of esters at both phenol hydroxy groups. We carried out the reaction of compound (+)-**2** with Boc_2O, which is generally used for the introduction of the *tert*-butoxycarbonyl groups, which are stable in basic medium. The reaction resulted in the product (+)-**3** with the Boc-protected hydroxy groups in nearly quantitative yield (see Scheme 1). However, it turned out that compound (+)-**3** cannot be involved into condensation with benzaldehyde.

Another widely used approach to the protection of phenol hydroxy groups consists in their methylation with diazomethane. The reaction of compound (+)-**2** with diazomethane led to the product (+)-**4** bearing a methylated phenol hydroxyl at position 9 in 55% yield (Scheme 2). In this case, ring C in compound (+)-**2** was also involved into transformation: it underwent ring-expansion, and its carbonyl group C(1)=O reacted with CH_2N_2 to give an oxirane ring. The reaction of compound (+)-**2** with diazomethane was carried out with a large excess of the latter, since a decrease in the ratio of the reactant and the substrate even to 10 : 1 led to the incomplete conversion of the substrate. Note that even the use of a large excess of diazomethane leaves the phenol hydroxyl at the C(7) atom unmethylated. Taking into account the literature data,[10] this phenomenon can be presumably accounted for by the presence of the closely positioned carbonyl group C(13)=O, whose oxygen atom forms a strong hydrogen bond with the proton of the OH group at the atom C(7). Since the phenol hydroxyl at the atom C(9) in compound (+)-**2** is also involved into the hydrogen bonding[11] and yet is methylated in the reaction course, we can suggest that, apparently, the transformation of ring C occurs initially, which destroys the hydrogen bond between the hydrogen of the phenol hydroxyl at the atom C(9) and the oxygen atom of the carbonyl group C(1)=O, and then this phenol hydroxyl undergoes unimpeded methylation. This is also confirmed by the data in the work,[11] in which the authors were intended to methylate the phenol hydroxy groups of usnic acid upon treatment with diazomethane, but did not isolate the target products, possibly, for the reason that both OH groups are involved into the hydrogen bonding.[12]

Scheme 2



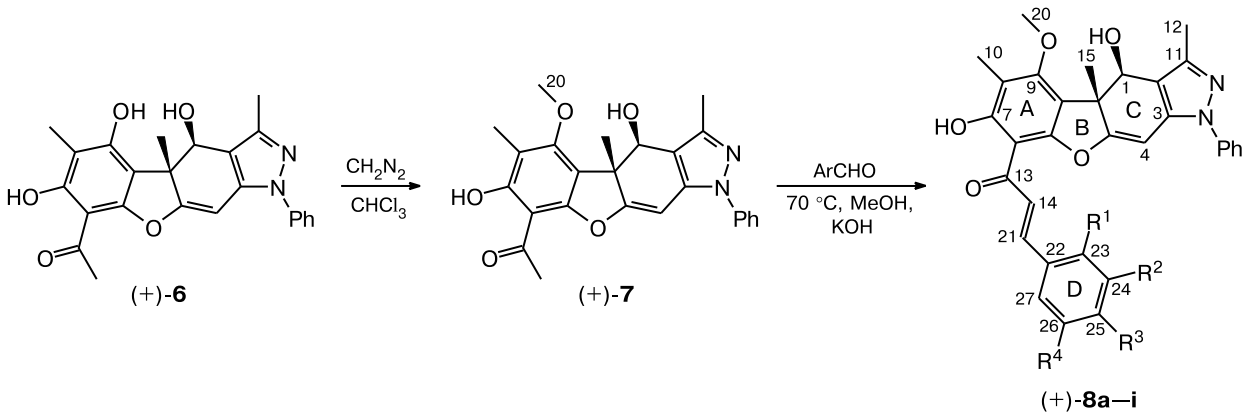
Based on the reaction mechanism of diazomethane with cyclic carbonyl compounds, we can suggest that expansion of ring C in compound (+)-**2** takes place initially, then the oxirane ring is formed from the carbonyl group C(1)=O, which is followed by the methylation of the phenol hydroxyl. Thus, three different sequential reactions take place upon the action of diazomethane on compound (+)-**2**, which is quite unusual, and earlier[13] has not been mentioned in the literature. In addition, the process is stereoselective and gives only one stereoisomer of compound (+)-**4** (the NMR spectra contain a single set of signals).

The condensation of compound (+)-**4** with benzaldehydes in methanol in the presence of aqueous KOH leads to chalcones (+)-**5a,b** in 21 and 31% yields, respectively, and a complete conversion of the substrate (see Scheme 2). Possibly, the presence of the labile exocyclic oxirane fragment is the reason for the low yields and considerable resinification in this reaction.

Earlier,[14] we have shown that the pyrazole derivative (+)-**2** is regioselectively reduced at the carbonyl group C(1)=O upon the action of $NaBH_4$ to give compound (+)-**6** in 94% yield. Treatment of the latter with diazomethane leads to the product (+)-**7** monomethylated at the phenol hydroxyl at the atom C(9) in 80% yield (Scheme 3). Thus, we consider compound **7** to be more promising substrate for the synthesis of chalcones as compared to the unstable derivatives **4**.

The condensation of compound (+)-**7** with benzaldehydes in methanol (70 °C, 2.5—3 h) in the presence of

Scheme 3



8	R^1	R^2	R^3	R^4	Yield (%)	**8**	R^1	R^2	R^3	R^4	Yield (%)	**8**	R^1	R^2	R^3	R^4	Yield (%)
a	H	H	H	H	77	**d**	H	H	OMe	H	70	**g**	H	NO_2	H	H	40
b	H	H	F	H	77	**e**	F	H	H	H	46	**h**	H	OMe	OMe	OMe	58
c	H	H	Cl	H	61	**f**	OMe	H	H	H	68	**i**	H	OMe	OMe	H	60

aqueous KOH led to the expected chalcones (+)-**8a—i** (see Scheme 3).

The highest yields were observed in the reactions with unsubstituted benzaldehyde ((+)-**8a**) and with benzaldehydes containing methoxy groups at the *para*- and *ortho*-positions ((+)-**8d**,**f**). An increase in the number of methoxy substituents in benzaldehyde leads to a decrease in the yields of chalcones ((+)-**8h**,**i**), the same is true if a fluorine atom is present at the *ortho*-position of benzaldehyde ((+)-**8e**). Benzaldehyde with a strong acceptor, nitro group at the *meta*-position, reacts with compound (+)-**7** at room temperature, but the yield of chalcone (+)-**8g** has proved the lowest in the series of interest. In the case of 4-dimethylaminobenzaldehyde bearing a strong electron-donating substituent, the aldehyde is predominantly involved into the Cannizzaro reaction. The similar approach was used for the preparation of chalcones (−)-**8a—i** based on the acid (−)-**1**.

In conclusion, we have developed a four-step synthesis of chalcones based on (+)- and (−)-usnic acids. Nine pares of enantiomeric chalcones ((+)- and (−)-**8a—i**) with different substituents in ring D have been synthesized.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer (400.13 and 100.61 MHz, respectively) for solutions of compounds in $CDCl_3$. Residual signals of the solvent were used as references (δ_H 7.24, δ_C 76.90). Mass spectra (70 eV) were recorded on a DFS Thermo Scientific high resolution mass spectrometer. Melting points were measured on a Kofler heating stage. Specific rotation is given in (deg mL) (g dm)$^{-1}$, concentration of solutions, in g (100 mL)$^{-1}$.

(+)-Usnic acid ((+)-**1**) ($[\alpha]_D^{20}$ +478 (*c* 0.1, $CHCl_3$)) was isolated from the lichens mixture of the *Usnea* family, (−)-usnic acid ((−)-**1**) ($[\alpha]_D^{20}$ −458 (*c* 0.1, $CHCl_3$)), from the lichen *Cladonia Stellaris* according to the known procedure.[15] Compound (+)-**2** was synthesized according to the described procedure.[16] Sodium borohydride was purchased from EvroKhim-Proekt Ltd. Merck silica gel (63—200μ) was used for column chromatography. Thin-layer chromatography was performed on Sorbfil plates (UV-254).

The atom numeration in compounds (see Schemes 1—3) is given for the assignment of signals in the NMR spectra and sometimes differ from the atom numeration in the nomenclature names. Spectral characteristics are given only for compounds (+)-**7** and (+)-**8a—i**, derived from (+)-**1**. For their enantiomers, derived from (−)-**1**, nomenclature names and values of specific rotation are only given.

(*S*)-8-Acetyl-5,7-di(*tert*-butoxycarbonyloxy)-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-4-one ((+)-3). Triethylamine (1 mL), a small crystal of DMAP, and Boc_2O (6 mmol) were added to a solution of compound (+)-**2** (1 mmol) in diethyl ether (5 mL), the mixture was stirred at room temperature until the substrate was completely converted (TLC monitoring). The reaction mixture was washed with water, dried with $MgSO_4$, the solvent was evaporated, and the residue was subjected to chromatography on a silica gel column (eluent $CHCl_3$). The yield was 95%, m.p. 93—95 °C, $[\alpha]_D^{30}$ +211 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.48, 1.53 (both s, 18 H, H(24), H(24′), H(24″), H(25), H(25′), H(25″)); 1.83 (s, 3 H, H(15)); 2.04 (s, 3 H, H(10)); 2.48 (s, 3 H, H(12)); 2.53 (s, 3 H, H(14)); 6.14 (s, 1 H, H(4)); 7.39 (s, 1 H, H(19)); 7.43—7.54 (m, 4 H, H(17), H(17′), H(18), H(18′)). ^{13}C NMR, δ: 9.42 (C(15)); 12.80 (C(12)); 27.47, 27.59 (C(24), C(24′), C(24″), C(25), C(25′), C(25″)); 29.30 (C(10)); 31.73 (C(14)); 60.58 (C(9b)); 83.96, 84.11 (C(22), C(23)); 89.30 (C(4)); 110.81 (C(9a)); 115.69 (C(6)); 119.30 (C(8)); 122.49 (C(2)); 123.57 (C(17), C(17′)); 128.12 (C(19)); 129.41 (C(18), C(18′)); 138.06 (C(16)); 145.30 (C(11)); 146.60 (C(3)); 147.87 (C(5a)); 148.19 (C(7)); 150.79, 150.67 (C(20), C(21)); 154.16 (C(9)); 171.22 (C(4a)); 190.39 (C(1)); 195.07 (C(13)). HRMS, found: *m*/*z* 616.2410 $[M]^+$. $C_{34}H_{36}N_2O_9$. Calculated: M = 616.2415.

Reactions of compounds (+)-2 and (+)-6 with diazomethane (general procedure). A solution of diazomethane (prepared from *N*-methyl-*N*-nitrosourea (2 g)) was carefully added to a solution of compound (+)-**2** or (+)-**6** (1 mmol) in chloroform (5 mL) with stirring, and the reaction mixture was kept at room temperature until evolution of the gas ceased, then the solvent was evaporated, and the residue was subjected to chromatography on a silica gel column (60—200μ, eluent chloroform) to obtain compounds (+)-**4** and (+)-**7**, respectively.

(5a*S*)-9-Acetyl-8-hydroxy-6-methoxy-3,5a,7-trimethyl-1-phenyl-4,5a-dihydro-1*H*-spiro[benzofuro[3′,2′:5,6]cyclohepta-[1,2-*c*]pyrazole-5,2′-oxirane] ((+)-4). The yield was 55%, m.p. 112—114 °C. ^{1}H NMR, δ: 1.73 (s, 3 H, H(15)); 2.11 (s, 3 H, H(10)); 2.14 (dd, 1 H, H(21)$_\alpha$, ^2J = 4.7 Hz, $J_{21,1a}$ = 2.0 Hz); 2.24 (s, 3 H, H(12)); 2.39 (d, 1 H, H(4)$_\beta$, ^2J = 17.0 Hz); 2.44 (d, 1 H, H(12)$_\beta$, ^2J = 4.7 Hz); 2.61 (s, 3 H, H(14)); 3.66 (dd, 1 H, H(1a)$_\alpha$, ^2J = 17.0 Hz, $J_{1a,21}$ = 2.0 Hz); 3.93 (s, 3 H, OCH_3); 6.10 (s, 1 H, H(4)); 7.34—7.38 (m, 1 H, H(19)); 7.42—7.50 (m, 4 H, H(17), H(17′), H(18), H(18′)); 13.30 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.66 (C(10)); 11.57 (C(12)); 17.95 (C(15)); 30.17 (C(1a)); 31.44 (C(14)); 50.84 (C(21)); 52.07 (C(9b)); 58.15 (C(1)); 61.63 (C(20)); 91.95 (C(4)); 102.86 (C(6)); 111.30 (C(9a)); 111.35 (C(3)); 112.75 (C(8)); 125.19 (C(17), C(17′)); 127.43 (C(19)); 129.06 (C(18), C(18′)); 133.33 (C(2)); 139.37 (C(16)); 147.90 (C(11)); 156.49 (C(5a)); 163.13 (C(9)); 163.61 (C(7)); 163.78 (C(9a)); 201.62 (C(13)). HRMS, found: *m/z* 458.1835 [M]$^+$. $C_{27}H_{26}N_2O_5$. Calculated: M = 458.1836.

(4*S*,4a*R*)-8-Acetyl-4,7-dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazole ((+)-7). The yield was 80%, m.p. 78—79 °C, $[\alpha]_D^{20}$ +218 (*c* 0.3, $CHCl_3$). ^{1}H NMR, δ: 1.48 (s, 3 H, H(15)); 2.13 (s, 3 H, H(10)); 2.44 (s, 3 H, H(12)); 2.67 (s, 3 H, H(14)); 3.94 (s, 3 H, OCH_3); 3.97 (s, 1 H, C(1)OH); 5.40 (s, 1 H, H(1)); 5.96 (s, 1 H, H(4)); 7.30—7.51 (m, 5 H, H arom.); 13.26 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 8.94 (C(10)); 12.49 (C(12)); 17.77 (C(15)); 31.30 (C(14)); 52.00 (C(9b)); 61.49 (C(20)); 74.21 (C(1)); 89.93 (C(4)); 103.92 (C(6)); 111.96 (C(2)); 112.05 (C(9a)); 114.77 (C(8)); 122.66 (C(17), C(17′)); 126.55 (C(19)); 128.83 (C(18), C(18′)); 136.01 (C(16)); 138.86 (C(3)); 147.52 (C(11)); 157.63 (C(5a)); 159.36 (C(9)); 162.86 (C(7)); 166.71 (C(4a)); 201.59 (C(13)). HRMS, found: *m/z* 432.1678 [M]$^+$. $C_{25}H_{24}N_2O_5$. Calculated: M = 432.16797.

(4*R*,4a*S*)-8-Acetyl-4,7-dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazole ((−)-7). M.p. 80 °C, $[\alpha]_D^{20}$ −203 (*c* 0.2, $CHCl_3$).

Reactions of compounds (+)-4 and (+)-7 with substituted benzaldehydes (general procedure). A 50% aqueous KOH (2 mL) was added to a solution of compound (+)-**4** or (+)-**7** (1 mmol) and the corresponding substituted benzaldehyde (4 mmol) in MeOH (16 mL). The mixture was heated for 2.5—3 h at 70 °C (in the case of 3-nitrobenzaldehyde, at 20 °C). The substrate conversion was monitored by TLC, using the hexane—diethyl ether (7 : 3) mixture as an eluent. The reaction mixture was poured into cold water (100 mL), acidified with 10% aq. AcOH to pH ~5, extracted with CH_2Cl_2 (3×30 mL). The combined extract was dried with calcined $MgSO_4$, the solvent was evaporated, and the residue was subjected to chromatography on a silica gel column (60—200μ), using the CH_2Cl_2—MeOH (to 0.5%) mixture as an eluent to obtain compounds (+)-**5a**,**b** and (+)-**8a**—**i**.

(5a*S*)-8-Hydroxy-6-methoxy-3,5a,7-trimethyl-9-(1-oxo-3-phenylprop-2(*E*)-en-1-yl)-1-phenyl-4,5a-dihydro-1*H*-spiro-[benzofuro[3′,2′:5,6]cyclohepta[1,2-*c*]pyrazole-5,2′-oxirane] ((+)-5a). The yield was 21%, m.p. 125—127 °C, $[\alpha]_D^{30}$ +130 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.76 (s, 3 H, H(15)); 2.15 (s, 3 H, H(10)); 2.19 (dd, 1 H, H(21)$_\alpha$, ^2J = 4.7 Hz, $J_{21,1a}$ = 2.0 Hz); 2.25 (s, 3 H, H(12)); 2.38 (d, 1 H, H(4)$_\beta$, ^2J = 17.0 Hz); 2.46 (d, 1 H, H(12)$_\beta$, ^2J = 4.7 Hz); 3.68 (dd, 1 H, H(1a)$_\alpha$, ^2J = 17.0 Hz, $J_{1a,21}$ = = 2.0 Hz); 3.95 (s, 3 H, OCH_3); 6.19 (s, 1 H, H(4)); 7.28—7.59 (m, 10 H, H(17), H(17′), H(18), H(18′), H(19), H(24), H(24′), H(25), H(25′), H(26)); 7.85 (d, 1 H, H(14), *J* = 15.5 Hz); 7.93 (d, 1 H, H(22), *J* = 15.5 Hz); 13.90 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.53 (C(10)); 11.33 (C(12)); 17.69 (C(15)); 29.88 (C(1a)); 50.57 (C(21)); 51.69 (C(9b)); 57.92 (C(1)); 61.41 (C(20)); 91.72 (C(4)); 102.94 (C(6)); 111.14 (C(3)); 111.16 (C(9a)); 112.77 (C(8)); 124.73 (C(17), C(17′)); 124.99 (C(14)); 127.09 (C(19)); 128.20 (C(24), C(24′)); 128.47 (C(25), C(25′)); 128.65 (C(18), C(18′)); 130.20 (C(26)); 132.90 (C(2)); 134.55 (C(23)); 139.02 (C(16)); 143.96 (C(22)); 147.67 (C(11)); 155.59 (C(5a)); 162.98 (C(9)); 163.21 (C(9a)); 164.55 (C(7)); 190.80 (C(13)). HRMS, found: *m/z* 546.2150 [M]$^+$. $C_{34}H_{30}N_2O_5$. Calculated: M = 546.2141.

(5a*S*)-8-Hydroxy-6-methoxy-3,5a,7-trimethyl-9-[1-oxo-3-(4-chlorophenyl)prop-2(*E*)-en-1-yl]-1-phenyl-4,5a-dihydro-1*H*-spiro[benzofuro[3′,2′:5,6]cyclohepta[1,2-*c*]pyrazole-5,2′-oxirane] ((+)-5b). The yield was 31%, m.p. 110—113 °C, $[\alpha]_D^{30}$ +147 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.76 (s, 3 H, H(15)); 2.14 (s, 3 H, H(10)); 2.19 (dd, 1 H, H(21)$_\alpha$, ^2J = 4.7 Hz, $J_{21,1a}$ = 2.0 Hz); 2.25 (s, 3 H, H(12)); 2.41 (d, 1 H, H(4)$_\beta$, ^2J = 17.0 Hz); 2.46 (d, 1 H, H(12)$_\beta$, ^2J = 4.7 Hz); 3.68 (dd, 1 H, H(1a)$_\alpha$, ^2J = 17.0 Hz, $J_{1a,21}$ = 2.0 Hz); 3.95 (s, 3 H, OCH_3); 6.15 (s, 1 H, H(4)); 7.22—7.52 (m, 9 H, H(17), H(17′), H(18), H(18′), H(19), H(24), H(24′), H(25), H(25′)); 7.77 (d, 1 H, H(14), *J* = 15.6 Hz); 7.87 (d, 1 H, H(22), *J* = 15.6 Hz); 13.82 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.83 (C(10)); 11.60 (C(12)); 17.97 (C(15)); 30.15 (C(1a)); 50.86 (C(21)); 52.00 (C(9b)); 58.21 (C(1)); 61.72 (C(20)); 92.05 (C(4)); 103.17 (C(6)); 111.47 (C(3)); 111.52 (C(9a)); 113.13 (C(8)); 125.07 (C(17), C(17′)); 125.77 (C(14)); 127.52 (C(19)); 128.99 (C(18), C(18′)); 129.06 (C(25), C(25′)); 129.60 (C(24), C(24′)); 133.16 (C(2)); 133.35 (C(23)); 136.35 (C(26)); 139.27 (C(16)); 142.67 (C(22)); 147.99 (C(11)); 155.85 (C(5a)); 163.41 (C(9)); 163.50 (C(9a)); 164.85 (C(7)); 190.82 (C(13)). HRMS, found: *m/z* 580.1765 [M]$^+$. $C_{34}H_{29}ClN_2O_5$. Calculated: M = 580.1760.

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-phenylprop-2-en-1-one ((+)-8a). The yield was 77%, m.p. 120—122 °C, $[\alpha]_D^{20}$ +38 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.52 (s, 3 H, H(15)); 2.18 (s, 3 H, H(10)); 2.46 (s, 3 H, H(12)); 3.97 (s, 3 H, OCH_3); 4.04 (s, 1 H, C(1)OH); 5.44 (s, 1 H, H(1)); 6.01 (s, 1 H, H(4)); 7.31—7.63 (m, 10 H, H arom.); 7.93 (s, 2 H, H(14), H(21)); 13.91 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.44 (C(10)); 12.83 (C(12)); 18.13 (C(15)); 52.25 (C(9b)); 61.86 (C(20)); 74.49 (C(1)); 90.20 (C(4)); 104.63 (C(6)); 112.40 (C(2)); 112.72 (C(9a)); 115.16 (C(8)); 123.14 (C(17), C(17′)); 124.82 (C(14)); 126.89 (C(19)); 128.73 (C(18), C(18′)); 128.92 (C(23), C(27)); 129.21 (C(24), C(26)); 130.72 (C(25)); 134.71 (C(22)); 136.32 (C(16)); 139.24 (C(3)); 145.30 (C(21)); 147.89 (C(11)); 157.32 (C(5a)); 159.75 (C(9)); 164.48 (C(7)); 167.01 (C(4a)); 191.26 (C(13)). HRMS, found: *m/z* 520.1995 [M]$^+$. $C_{32}H_{28}N_2O_5$. Calculated: M = 520.1993.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-

phenylprop-2-en-1-one ((–)-8a). M.p. 121—122 °C, $[\alpha]_D^{20}$ –41 (*c* 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-fluorophenyl)prop-2-en-1-one ((+)-8b). The yield was 77%, m.p. 103—105 °C, $[\alpha]_D^{20}$ +57 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.51 (s, 3 H, H(15)); 2.16 (s, 3 H, H(10)); 2.46 (s, 3 H, H(12)); 3.96 (s, 3 H, OCH_3); 4.03 (s, 1 H, C(1)OH); 5.43 (s, 1 H, H(1)); 5.99 (s, 1 H, H(4)); 7.09 (m, 2 H, H(24)); 7.28—7.55 (m, 5 H, H arom.); 7.61 (m, 2 H, H(23)); 7.83 (d, 1 H, H(14), *J* =15.5 Hz); 7.90 (d, 1 H, H(21), *J* = 15.5 Hz); 14.05 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.42 (C(10)); 12.81 (C(12)); 18.12 (C(15)); 52.25 (C(9b)); 61.88 (C(20)); 74.52 (C(1)); 90.24 (C(4)); 104.57 (C(6)); 112.47 (C(2)); 112.78 (C(9a)); 115.25 (C(8)); 116.15 (d, C(24), C(26), $J_{C,F}$ = 21.9 Hz); 123.18 (C(17), C(17′)); 124.51 (C(14)); 126.94 (C(19)); 129.22 (C(18), C(18′)); 130.67 (d, C(23), C(27), $J_{C,F}$ = 8.2 Hz); 130.98 (d, C(22), $J_{C,F}$ = 3.3 Hz); 136.27 (C(16)); 139.24 (C(3)); 143.95 (C(21)); 147.90 (C(11)); 157.27 (C(5a)); 159.80 (C(9)); 164.11 (d, C(25), $J_{C,F}$ = 250.7 Hz); 164.49 (C(7)); 166.96 (C(4a)); 191.05 (C(13)). HRMS, found: *m/z* 538.1899 $[M]^+$. $C_{32}H_{27}FN_2O_5$. Calculated: M = 538.1890.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-fluorophenyl)prop-2-en-1-one ((–)-8b). M.p. 102—103 °C, $[\alpha]_D^{27}$ –75 (*c* 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-chlorophenyl)prop-2-en-1-one ((+)-8c). The yield was 61%, m.p. 111—114 °C, $[\alpha]_D^{20}$ +57 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.53 (s, 3 H, H(15)); 2.18 (s, 3 H, H(10)); 2.47 (s, 3 H, H(12)); 3.98 (s, 3 H, OCH_3); 4.04 (s, 1 H, C(1)OH); 5.45 (s, 1 H, H(1)); 6.00 (s, 1 H, H(4)); 7.27—7.58 (m, 9 H, H arom.); 7.85 (d, 1 H, H(14), *J* = 15.4 Hz); 7.90 (d, 1 H, H(21), *J* = 15.4 Hz); 13.87 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.42 (C(10)); 12.81 (C(12)); 18.12 (C(15)); 52.24 (C(9b)); 61.86 (C(20)); 74.47 (C(1)); 90.24 (C(4)); 104.55 (C(6)); 112.37 (C(2)); 112.78 (C(9a)); 115.20 (C(8)); 123.14 (C(17), C(17′)); 125.24 (C(14)); 126.95 (C(19)); 129.20 (C(18), C(18′)); 129.23 (C(24), C(26)); 129.81 (C(23), C(27)); 133.18 (C(22)); 136.24 (C(16)); 136.63 (C(25)); 139.19 (C(3)); 143.71 (C(21)); 147.88 (C(11)); 157.27 (C(5a)); 159.87 (C(9)); 164.49 (C(7)); 166.93 (C(4a)); 190.96 (C(13)). HRMS, found: *m/z* 554.1603 $[M]^+$. $C_{32}H_{27}ClN_2O_5$. Calculated: M = 554.1587.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-chlorophenyl)prop-2-en-1-one ((–)-8c). M.p. 112—113 °C, $[\alpha]_D^{27}$ –68 (*c* 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-methoxyphenyl)prop-2-en-1-one ((+)-8d). The yield was 70%, m.p. 105—107 °C, $[\alpha]_D^{20}$ +23 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.50 (s, 3 H, H(15)); 2.14 (s, 3 H, H(10)); 2.45 (s, 3 H, H(12)); 3.81, 3.94 (both s, 3 H each, OCH_3); 4.05 (s, 1 H, C(1)OH); 5.42 (s, 1 H, H(1)); 5.97 (s, 1 H, H(4)); 6.89 (d, 2 H, H(23), *J* = 8.65 Hz); 7.29—7.58 (m, 7 H, H arom.); 7.77 (d, 1 H, H(14), *J* = 15.5 Hz); 7.87 (d, 1 H, H(21), *J* = 15.5 Hz); 14.06 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.40 (C(10)); 12.83 (C(12)); 18.14 (C(15)); 52.20 (C(9b)); 55.31 (C(28)); 61.82 (C(20)); 74.43 (C(1)); 90.07 (C(4)); 104.62 (C(6)); 112.38 (C(2)); 112.65 (C(9a)); 114.38 (C(24), C(26)); 115.01 (C(8)); 122.28 (C(14)); 123.11 (C(17), C(17′)); 126.85 (C(19)); 127.42 (C(22)); 129.23 (C(18), C(18′)); 130.63 (C(23), C(27)); 136.35 (C(16)); 139.26 (C(3)); 145.28 (C(21)); 147.86 (C(11)); 157.16 (C(5a)); 159.44 (C(9)); 161.85 (C(25)); 164.46 (C(7)); 167.09 (C(4a)); 191.04 (C(13)). HRMS, found: *m/z* 550.2099 $[M]^+$. $C_{33}H_{30}N_2O_6$. Calculated: M = 550.2098.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(4-methoxyphenyl)prop-2-en-1-one ((–)-8d). M.p. 105—106 °C, $[\alpha]_D^{19}$ –57 (*c* 0.4, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(2-fluorophenyl)prop-2-en-1-one ((+)-8e). The yield was 46%, m.p. 93—96 °C, $[\alpha]_D^{27}$ +96 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.52 (s, 3 H, H(15)); 2.16 (s, 3 H, H(10)); 2.47 (s, 3 H, H(12)); 3.97 (s, 3 H, OCH_3); 4.04 (d, 1 H, C(1)OH, *J* = 1.3 Hz); 5.44 (s, 1 H, H(1)); 5.99 (s, 1 H, H(4)); 7.08 (m, 1 H, H(24)); 7.13 (m, 1 H, H(26)); 7.31—7.50 (m, 6 H, H arom.); 7.61 (m, 1 H, H(25)); 7.99 (d, 1 H, H(14), *J* = 15.6 Hz); 8.06 (d, 1 H, H(21), *J* = 15.6 Hz); 13.85 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.39 (C(10)); 12.80 (C(12)); 18.08 (C(15)); 52.23 (C(9b)); 61.83 (C(20)); 74.43 (C(1)); 90.17 (C(4)); 104.57 (C(6)); 112.40 (C(2)); 112.69 (C(9a)); 115.17 (C(8)); 116.22 (d, C(24), $J_{C,F}$ = 21.9 Hz); 122.87 (d, C(22), $J_{C,F}$ = 11.6 Hz); 123.05 (C(17), C(17′)); 124.45 (d, C(14), $J_{C,F}$ = 3.6 Hz); 126.84 (C(19)); 127.30 (d, C(26), $J_{C,F}$ = 7.3 Hz); 129.18 (C(18), C(18′)); 129.86 (d, C(27), $J_{C,F}$ = 2.9 Hz); 132.02 (d, C(25), $J_{C,F}$ = 8.6 Hz); 136.29 (C(16)); 137.70 (d, C(21), $J_{C,F}$ = 2.0 Hz); 139.23 (C(3)); 147.85 (C(11)); 157.33 (C(5a)); 159.85 (C(9)); 160 (d, C(23), $J_{C,F}$ = 255.4 Hz); 164.48 (C(7)); 166.96 (C(4a)); 191.16 (C(13)). HRMS, found: *m/z* 538.1902 $[M]^+$. $C_{33}H_{30}N_2O_6$. Calculated: M = 538.1899.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(2-fluorophenyl)prop-2-en-1-one ((–)-8e). M.p. 94—96 °C, $[\alpha]_D^{20}$ –109 (*c* 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(2-methoxyphenyl)prop-2-en-1-one ((+)-8f). The yield was 68%, m.p. 99—103 °C, $[\alpha]_D^{20}$ +81 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.52 (s, 3 H, H(15)); 2.17 (s, 3 H, H(10)); 2.47 (s, 3 H, H(12)); 3.89 (s, 3 H, OCH_3); 3.97 (s, 3 H, OCH_3); 4.06 (d, 1 H, C(1)OH, *J* = 1.3 Hz); 5.45 (s, 1 H, H(1)); 5.99 (s, 1 H, H(4)); 6.92 (d, 1 H, H(26), *J* = 8.3 Hz); 6.98 (m, 1 H, H(24)); 7.31—7.60 (m, 6 H, H arom.); 7.63 (m, 1 H, H(23)); 8.04 (d, 1 H, H(14), *J* = 15.7 Hz); 8.28 (d, 1 H, H(21), *J* = 15.7 Hz); 14.07 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.42 (C(10)); 12.83 (C(12)); 18.12 (C(15)); 52.27 (C(9b)); 55.39 (C(28)); 61.82 (C(20)); 74.51 (C(1)); 89.99 (C(4)); 104.74 (C(6)); 111.13 (C(24)); 112.41 (C(2)); 112.63 (C(9a)); 115.02 (C(8)); 120.70 (C(26)); 123.02 (C(17), C(17′)); 123.76 (C(22)); 125.21 (C(14)); 126.84 (C(19)); 129.14 (C(18), C(18′)); 129.25 (C(25)); 132.08 (C(27)); 136.37 (C(16)); 139.25 (C(3)); 140.72 (C(21)); 147.89 (C(11)); 157.31 (C(5a)); 158.87 (C(23)); 159.53 (C(9)); 164.50 (C(7)); 167.15 (C(4a)); 191.67 (C(13)). HRMS, found: *m/z* 550.2091 $[M]^+$. $C_{33}H_{30}N_2O_6$. Calculated: M = 550.2098.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(2-methoxyphenyl)prop-2-en-1-one ((–)-8f). M.p. 100—103 °C, $[\alpha]_D^{20}$ –73 (*c* 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3-nitrophenyl)prop-2-en-1-one ((+)-8g). The yield was 40%, m.p. 95—98 °C, $[\alpha]_D^{27}$ +85 (*c* 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.52 (s, 3 H, H(15)); 2.17 (s, 3 H, H(10)); 2.45 (s, 3 H, H(12)); 3.97

(s, 3 H, OCH_3); 4.01 (s, 1 H, C(1)OH); 5.44 (s, 1 H, H(1)); 6.09 (s, 1 H, H(4)); 7.07—7.63 (m, 9 H, H arom.); 7.86 (d, 1 H, H(14), J = 15.6 Hz); 8.06 (d, 1 H, H(21), J = 15.6 Hz); 13.62 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.07 (C(10)); 12.48 (C(12)); 17.75 (C(15)); 52.00 (C(9b)); 61.57 (C(20)); 74.15 (C(1)); 90.26 (C(4)); 104.16 (C(6)); 112.06 (C(2)); 112.53 (C(9a)); 115.12 (C(8)); 122.55 (C(23)); 122.65 (C(17), C(17′)); 124.30 (C(25)); 126.62 (C(19)); 127.66 (C(14)); 128.94 (C(18), C(18′)); 129.65 (C(26)); 134.01 (C(27)); 135.76 (C(22)); 136.24 (C(16)); 138.81 (C(3)); 141.14 (C(21)); 147.52 (C(11)); 148.31 (C(24)); 157.08 (C(5a)); 159.96 (C(9)); 164.10 (C(7)); 166.32 (C(4a)); 190.33 (C(13)). HRMS, found: m/z 565.1848 $[M]^+$. $C_{32}H_{27}N_3O_7$. Calculated: M = 565.1844.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3-nitrophenyl)prop-2-en-1-one ((−)-8g). M.p. 95—97 °C, $[\alpha]_D^{27}$ −79 (c 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one ((+)-8h). The yield was 58%, m.p. 119—121 °C, $[\alpha]_D^{20}$ +23 (c 0.2, $CHCl_3$). ^{1}H NMR, δ: 1.49 (s, 3 H, H(15)); 2.12 (s, 3 H, H(10)); 2.44 (s, 3 H, H(12)); 3.83 (s, 6 H, 2 OCH_3); 3.87, 3.95 (both s, 3 H each, OCH_3); 3.96 (s, 1 H, C(1)OH); 5.40 (s, 1 H, H(1)); 5.86 (s, 1 H, H(4)); 6.82 (s, 2 H, H(23), H(27)); 7.28—7.50 (m, 5 H, H arom.); 7.74 (d, 1 H, H(14), J = 15.3 Hz); 7.91 (d, 1 H, H(21), J = 15.3 Hz); 13.90 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.34 (C(10)); 12.81 (C(12)); 18.04 (C(15)); 52.35 (C(9b)); 55.76 (C(28), C(28′)); 60.88 (C(29)); 61.80 (C(20)); 74.49 (C(1)); 89.73 (C(4)); 104.55 (C(6)); 105.62 (C(23), C(27)); 112.35 (C(2)); 112.75 (C(9a)); 115.07 (C(8)); 122.89 (C(17), C(17′)); 124.44 (C(14)); 126.95 (C(19)); 129.03 (C(18), C(18′)); 130.24 (C(22)); 136.09 (C(16)); 139.13 (C(3)); 40.52 (C(25)); 144.71 (C(21)); 147.92 (C(11)); 153.24 (C(24), C(26)); 157.17 (C(5a)); 159.71 (C(9)); 164.49 (C(7)); 166.85 (C(4a)); 190.89 (C(13)). HRMS, found: m/z 610.2303 $[M]^+$. $C_{35}H_{34}N_2O_8$. Calculated: M = 610.2310.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one ((−)-8h). M.p. 118—121 °C, $[\alpha]_D^{20}$ −29 (c 0.2, $CHCl_3$).

(*E*)-1-[(4*S*,4a*R*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3,4-dimethoxyphenyl)prop-2-en-1-one ((+)-8i). The yield was 60%, m.p. 115—117 °C, $[\alpha]_D$ +19 (c 0.3, $CHCl_3$). ^{1}H NMR, δ: 1.52 (s, 3 H, H(15)); 2.17 (s, 3 H, H(10)); 2.47 (s, 3 H, H(12)); 3.83, 3.87 (both s, 6 H, 2 OCH_3); 3.98 (s, 3 H, OCH_3); 4.04 (s, 1 H, C(1)OH); 5.46 (s, 1 H, H(1)); 5.94 (s, 1 H, H(4)); 6.89 (d, 1 H, H(26), J = 8.4 Hz); 7.16 (s, 1 H, H(23)); 7.22 (d, 1 H, H(27), J = 8.4 Hz); 7.34 (m, 1 H, H(19)); 7.49 (m, 4 H, H(17), H(17′), H(18), H(18′)); 7.86 (d, 1 H, H(14), J = 15.7 Hz); 7.90 (d, 1 H, H(21), J = 15.7 Hz); 14.05 (s, 1 H, C(7)OH). ^{13}C NMR, δ: 9.37 (C(10)); 12.79 (C(12)); 18.08 (C(15)); 52.30 (C(9b)); 55.45, 55.88 (C(28), C(29)); 61.79 (C(20)); 74.47 (C(1)); 89.79 (C(4)); 104.60 (C(6)); 110.03, 111.02 (C(23), C(26)); 112.37, 112.69 (C(2), C(9a)); 115.00 (C(8)); 122.83 (C(27)); 122.98 (C(17), C(17′)); 123.49 (C(14)); 126.87 (C(19)); 127.75 (C(22)); 129.08 (C(18), C(18′)); 136.21 (C(16)); 139.18 (C(3)); 145.07 (C(21)); 147.90 (C(25)); 149.01 (C(24)); 151.58 (C(11)); 157.17 (C(5a)); 159.52 (C(9)); 164.49 (C(7)); 167.00 (C(4a)); 190.93 (C(13)). HRMS, found: m/z 580.2190 $[M]^+$. $C_{34}H_{32}N_2O_7$. Calculated: M = 580.2204.

(*E*)-1-[(4*R*,4a*S*)-4,7-Dihydroxy-5-methoxy-3,4a,6-trimethyl-1-phenyl-4,4a-dihydro-1*H*-benzofuro[3,2-*f*]indazol-8-yl]-3-(3,4-dimethoxyphenyl)prop-2-en-1-one ((−)-8i). M.p. 115—118 °C, $[\alpha]_D^{27}$ −24 (c 0.2, $CHCl_3$).

References

1. D. Batovska, I. Todorova, *Curr. Clin. Pharm.*, 2010, **5**, 1.
2. S. Vogel, S. Ohmayer, G. Brunner, J. Heilmann, *Bioorg. Med. Chem.*, 2008, **16**, 4286.
3. O. Petrov, Y. Ivanova, M. Gerova, *Catal. Commun.*, 2008, **9**, 315.
4. K. Ingolfsdottir, *Phytochemistry*, 2002, **61**, 729.
5. N. K. Honda, F. R. Pavan, R. G. Coelho, S. R. de Andrade Leite, A. C. Micheletti, T. I. B. Lopes, M. Y. Misutsu, A. Beatriz, R. L. Brum, C. Q. F. Leite, *Phytomedicine*, 2010, **17**, 328.
6. H. Cetin, O. Tufan-Cetin, A. O. Turk, T. Tay, M. Candan, A. Yanikoglu, H. Sumbul, *Parasitol. Res.*, 2008, **102**, 1277.
7. K. Takahashi, M. Takani, *Chem. Pharm. Bull.*, 1980, **28**, 177.
8. E. Erba, D. Pocar, L. M. Rossi, *Il Farmaco*, 1998, **53**, 718.
9. J. P. Kutney, I. H. Sanchez, *Can. J. Chem.*, 1977, **55**, 1079.
10. *Protective Groups in Organic Chemistry*, Ed. J. F. W. McOmie, Premium Press, 1973, 387 pp.
11. L. Bertilsson, C. Wachtmeister, *Acta Chem. Scand.*, 1968, **22**, 3081.
12. V. Galasso, *Chem. Phys.*, 2010, **374**, 138.
13. Yu. V. Tomilov, V. A. Dokichev, U. M. Dzhemilev, O. M. Nefedov, *Usp. Khim.*, 1993, **62**, 847 [*Russ. Chem. Rev.* (*Engl. Transl.*), 1993, **62**].
14. D. N. Sokolov, O. A. Luzina, M. P. Polovinka, N. F. Salakhutdinov, *Khim. Prirodn. Soedin.*, 2011, No. 2, 188 [*Chem. Nat. Compd. (Engl. Transl.)*, 2011].
15. Pat. RF 2317076; *Byul. Isobret.* [*Invention Bull.*], 2008, No. 5.
16. M. Takai, Y. Uehara, J. A. Beisler, *J. Med. Chem.*, 1979, **22**, 1380.

Received May 10, 2011;
in revised form August 30, 2011