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Synthesis of 3-[(Coumarinyl)carbonyl]-3a,8b-dihyroindeno[1,2-b]pyrrole-4(1*H*)-ones and Their Conversion to Coumarin Bearing Spiro[isobenzofuran-1,2'-pyrrole] Moiety Compounds *via* Oxidative Cleavage Reaction

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New coumarin derivatives bearing indenopyrrole moiety were prepared by the reaction of salicylaldehyde, 4-hydroxy-6-methyl-2*H*-pyran-2-one, benzylamine and ninhydrin in the presence of triethylamine as a basic catalyst and the mentioned compounds lead to coumarin bearing spiro[isobenzofuran-1,2'-pyrrole] moiety compounds *via* an oxidative cleavage reaction by periodic acid. Ease of handling, easy purification and moderate to good yields are attractive features of the present method. The products also were characterized by IR, mass, elemental analyses, ^{1}H NMR, ^{13}C NMR and X-ray crystallography.

Coumarins are one of the most important oxygen-containing heterocyclic compounds and they are widely present in higher plants such as Apiaceae, Leguminosae, Thymelaeaceae, Rutaceae, Asteraceae, and they exist in microorganisms and animals. [1]Coumarins are playing important role in the realm of synthetic chemistry, biochemistry and natural products.[2] Due to their tremendous biological properties, coumarins are used as active component in pesticides,[3] and optical brightening agents.[4] Moreover, they can act as anticancer,[5] antioxidant,[6] antiviral,[7] inhibitory of platelet aggregation,[8] antifungal,[9] and anti-inflammatory agents.[10] It is proven that coumarins can play as inhibitor for some enzymes such as, aromatase,[11] horseradish peroxidase,[12] hAChE/BACE1[13] and 17β-hydroxysteroid dehydrogenase type 3.[14]

Due to these properties, coumarins have been given attention by chemists, and a range of methods have been reported for their synthesis including Baylis–Hillman reactions of salicylaldehyde,[15] Petasis reaction of salicylaldehydes,[16] reaction of α,β-unsaturated Fischer carbene complexes of chromium with propargyl ethers,[17] reaction of phenols with allenes containing ester groups,[18] olefin metathesis[19] and synthesis of coumarin from propargyl vinyl ethers.[20]

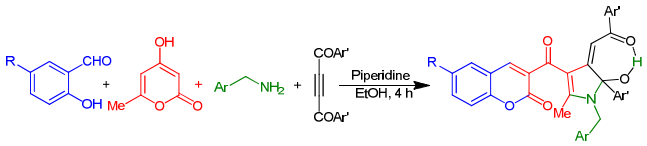
Accordingly, synthesis of new coumarin derivatives have been given attention by chemists and various methods have been developed for their synthesis.[21]

Spirocyclic frameworks represent an important class of naturally occurring compounds which have some biological properties.[22] Isobenzofuran-1(3*H*)-onesare oxygen-containing heterocyclic compounds which exhibiting a wide range of biological and pharmacological activities such as antimicrobial, anti arrahythmic, anti-platelet and anti-oxidant.[23] Moreover, this compound has been used as synthon for the synthesis of some biologically active heterocycle compounds.[24]

Accordingly, and because of their importance of isobenzofuran-1(3*H*)-ones and spirocyclic compounds, the preparation of spiroheterocyclic incorporation isobenzofuran-1(3*H*)-ones has been interested by chemists.[25]

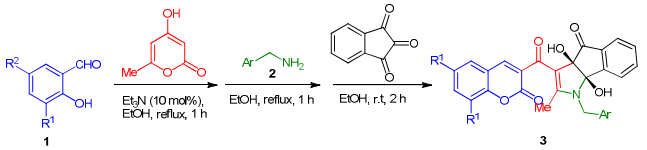
Against this background and our research program into the synthesis of new coumarin derivatives, very recently, we have reported the synthesis of novel [(1,2-dihydro-3*H*-pyrrol-4-yl)carbonyl]-2*H*-chromen-2-one (Scheme 1.)by using of 4-hydroxy-6-methyl-2*H*-pyran-2-one as an important reagent in synthesis of new coumarin derivatives based on a one-pot sequential four-component reaction.[26]

Scheme 1. Synthesis of [(1,2-dihydro-3*H*-pyrrol-4-yl)carbonyl]-2*H*-chromen-2-one



In recent years, multicomponent reactions (MCRs) have been given attention by chemists and these type of reactions are used to increase the molecular complexity and diversity with minimum time, cost and waste production.[27] So, incontinuation of our works on the synthesis of new coumarin derivatives,[28] herein we decided to synthesis substituted coumarin derivatives bearing indenopyrrole and spiro[isobenzofuran-1,2'-pyrrole]. We have observed that the sequential reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one, salicylaldehydes, benzylamines and ninhydrin in the presence of triethylamine in ethanol produced the substituted coumarin derivatives bearing indenopyrrole moiety (Scheme 2).

Scheme 2. Synthesis of coumarin bearing indenopyrrole moiety



The choice of an appropriate reaction medium is of crucial importance for successful synthesis. Initially, we chose the salicylaldehyde, 4-hydroxy-6-methyl-2*H*-pyran-2-one, benzylamine and ninhydrin as a model to establish the feasibility of the strategy and to optimize the reaction conditions. Different solvent, base and amount of base has been studied and the results are summarized in Table 1.

Table 1: Synthetic results of **3a** under different reaction conditions

Entry	Solvent	Base (mol %)	Yield %
1	EtOH	Et_3N (10%)	70
2	CH_3CN	Et_3N (10%)	40
3	THF	Et_3N (10%)	20
4	$CHCl_3$	Et_3N (10%)	15
5	EtOH	Et_3N (15%)	70
6	EtOH	Et_3N (5%)	63
7	EtOH	DABCO (10%)	70
8	EtOH	Piperidine (10%)	68
9	EtOH	K_2CO_3 (10%)	50
10	EtOH	-	-

The best results were obtained by performing the reaction in ethanol in the presence of 10 mol % of triethylamine as a catalyst to obtain the product **3a** in good yield (Table 1, entry 1). Performance of the reaction in the presence of DABCO and piperidine has the same result (Table 1, entry 7, 8) but we chose triethylamine as a milder catalyst for the reaction because triethylamine has low basicity in comparison of DABCO and piperidine. We also performed the model reaction in the absence of base but these failed to give thedesired product (Table 1, entry 10). It seems that base play an important role in the Knoevenagel condensation reaction between salicylaldehyde and 4-hydroxy-6-methyl-2*H*-pyran-2-one inthe first step.

After establishing optimal conditions, we explore the generality of the reaction for product **3**. For this purpose, we extended the reaction with various salicylaldehydes and benzylamines containing both electron withdrawing and electron-donating substituents. The reactions are generally clean and desired products **3a-g** was obtained in good yields. The results are summarized in Table 2.

Table 2: Prepared compound **3a-g**

Entry	Products	R^1	R^2	Ar	Yield %[a]
1	**3a**	H	H	C_6H_5	70
2	**3b**	H	H	4-ClC_6H_4	85
3	**3c**	H	H	4-$CH_3C_6H_4$	74
4	**3d**	H	H	4-$CH_3OC_6H_4$	65
5	**3e**	H	NO_2	4-$CH_3OC_6H_4$	80
6	**3f**	OCH_3	H	C_6H_5	75
7	**3g**	OCH_3	H	4-ClC_6H_4	87

[a]salicylaldehyde (1 mmol), 4-hydroxy-6-methyl-2*H*-pyran-2-one (1 mmol), benzylamine (1 mmol), ninhydrin (1 mmol), time (4 hours)

Our attempt to perform this protocol with various linear aliphatic amines failed to desired product **3** probably because of undesirable side reactions of linear aliphatic amines.[29a]

The molecular structures of all products **3a**–**g** were elucidated from their IR, elemental analyses, mass, ^{1}H NMR, and ^{13}C NMR spectra. The structure of **3a** was also confirmed by X-ray crystallography (Figure 1). The IR spectrum of **3a** showed absorption bands which are relatedto the two OH groups at 3412, the carbonyl groups at 1721, the C=C aromatic stretching at 1606, 1478 and 1414 and the C-O stretching at 1357 and 1184 cm^{-1}. The ^{1}H NMR spectrum of **3a** exhibited four sharp singlet signals (δ = 2.16, 6.05, 7.22 and 7.89 ppm), readily recognized as methyl, two OH and CH of chromene groups. Two benzylic CH_2 hydrogens have been shown two doublets (δ = 4.99, ^2J = 17.2 Hz) and (δ = 5.22, ^2J = 17.2 Hz) because they are diastereotopic. Twelve aromatic hydrogens gave rise to characteristic signals in the aromatic region of the spectrum. The ^{1}H-decoupled ^{13}C NMR spectrum of **3a** showed 27 distinct signals in agreement with the suggested structure. In the aliphatic region there is two resonances at δ = 14.51 and δ = 45.02 ppm which are related to the methyl and methylene groups. Signals due to CH_3-*C*=C, CO_2, CO and C^{4}O appeared at δ = 158.49, 163.98, 184.32 and 198.88 ppm respectively. The most important peaks is related to C-OH which appeared at δ = 83.94 and 105.78 ppm. Finally compound **3a** has been recrystallized from acetonitrile and X-ray analysis of this crystal confirms the structure. The ORTEP diagram of crystallography for compound **3a** is shown in Figure 1.

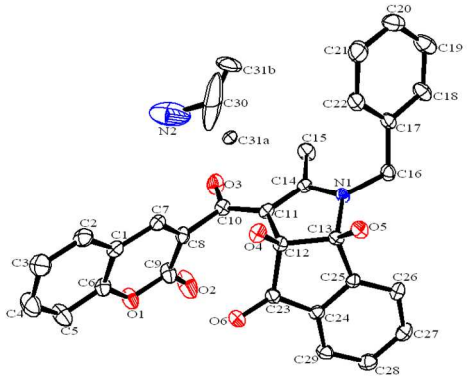
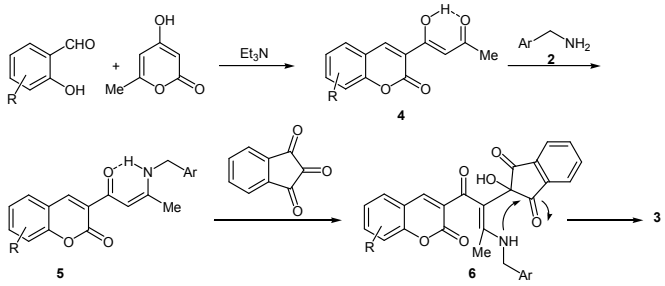


Figure 1: The molecular structure of compound **3a**.

Scheme 3. Proposed mechanism for the compound **3**



According to results, a plausible mechanism for the sequential four-component reaction is proposed (Scheme 3). At first, Knoevenagel condensation between salicylaldehyde **1** and 4-hydroxy-6-methyl-2*H*-pyran-2-one in the presence of triethylamine leads to the intermediate **4**.[29] Next, condensation

reaction between compound **4** and benzylamine **2** and imine-enamine tautomerization leads to enamine **5**. Finally nucleophilic addition of enamine **5** to ninhydrin and nitrogen cyclization gives desirable product **3**. To investigate the proposed mechanism, the intermediates **4a** and **5a** have been separated from the reaction mixture and their structure were established by ^{1}H NMR and ^{13}C NMR spectroscopy (see supporting information).

After the success to obtaining product **3**, we decided to perform oxidative cleavage on the compound **3** using H_5IO_6 as an oxidative reagent. For this purpose, the reaction between compound **3a** and periodic acid has been chosen as a model reaction to establish the feasibility of the strategy and to optimize the reaction conditions. Different solvent and temperatures has been studied and the results are summarized in Table 3.

Table 3. Synthetic results of **7a** under different reaction conditions

Entry	Solvent	Temperature (° C)	Time (h)	Yield (%)
1	CH_3CN	25	2	10
2	MeOH	25	2	54
3	**EtOH**	**25**	**2**	**88**
4	EtOH	45	2	72
5	EtOH	65	2	50
6	EtOH	78	2	34

The best results were obtained by performance the reaction in ethanol at 25 ºC for 2 h to obtain the product **7a** in good yield (Table 2, entry 3). Increasing temperature and also changing solvent lead to decrease the yield.

Table 4. Prepared compound **7a-g**

Entry	Products	R^1	R^2	Ar	Yield %[a]
1	**7a**	H	H	C_6H_5	88
2	**7b**	H	H	4-ClC_6H_4	82
3	**7c**	H	H	4-$CH_3C_6H_4$	75
4	**7d**	H	H	4-$CH_3OC_6H_4$	-
5	**7e**	H	NO_2	4-$CH_3OC_6H_4$	-
6	**7f**	OCH_3	H	C_6H_5	70
7	**7g**	OCH_3	H	4-ClC_6H_4	-

After establishing optimal conditions, we explore the generality of the reaction for product **7**. For this purpose, we used compound **3a-g** to extend the present method. The reactions are generally clean and desired products **7a-g** was obtained in good yields. The results are summarized in Table 4.

The molecular structures of all products **7a–c** and **7f** were assigned by IR, mass, ^{1}H-NMR, and ^{13}C-NMR spectra, and their elemental analyses, as described for **7a**. The mass spectrum of **7a** displays a peak at *m*/*z* 477 which is in good agreement with the proposed structure. In the IR spectrum of **7a**, absorption bands at 1795, 1721, 1690, 1634, 1502, 1191 and 1079 cm^{-1}, related to CO_2, C=O, C=C, and C-O stretching frequencies respectively, clearly indicated the most significant functional groups of the product. The ^{1}HNMR spectrum of **7a** shows two singlets at 2.88 and 8.06 ppm for OCH_3 and CH of chromene and two doublets at 4.54 and 4.81 ppm for CH_2. Thirteen aromatic hydrogens are also shown five doublets signals at 7.13, 7.36, 7.58, 7.77, 7.91, two triplets signals at 7.36, 7.71 and one multiplet signal at 7.14-7.34 ppm. The ^{1}H-decoupled ^{13}CNMR spectrum of **7a** showed 27 distinct signals in agreement with the suggested structure. In the aliphatic region there is three resonance at δ = 16.0, 46.5 and 94.3 ppm which is related to the Me, CH_2 and spirogroups. Resonance due to CO_2 and CO appeared at δ = 167.1, 182.9, 186.7 and 188.3 ppm respectively. Finally compounds **7a** has been recrystallized from acetonitrile and X-ray analysis of this crystal confirm the structure. The ORTEP diagram of crystallography for compound **7a** is shown in Figure 2.

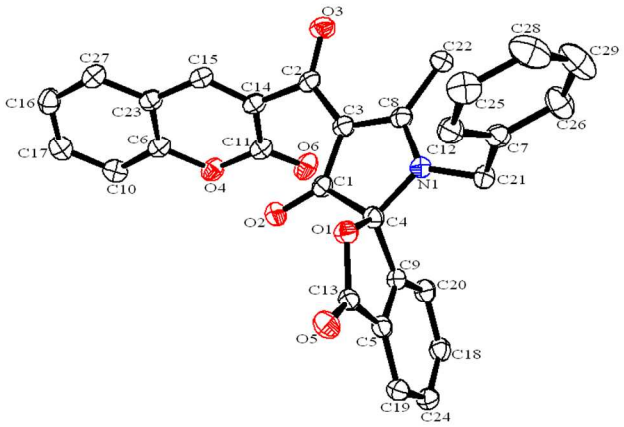


Figure 2. ORTEP diagram of **7a**

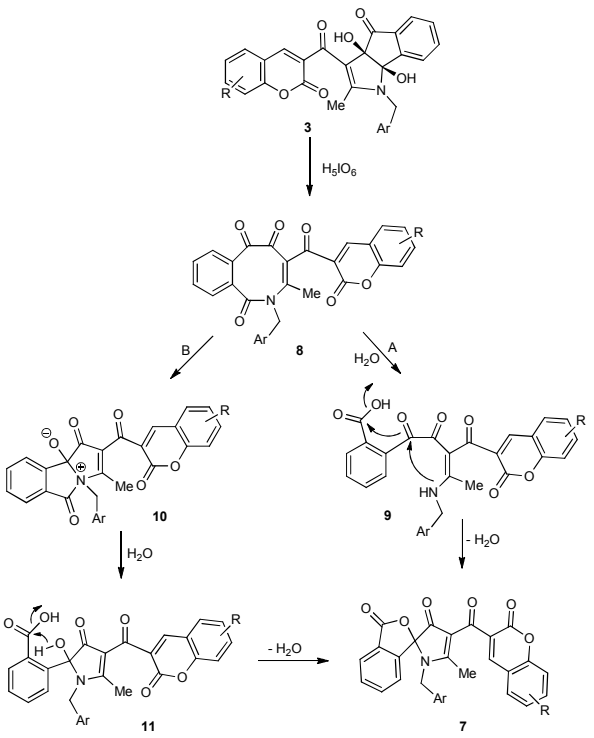
A plausible mechanism for the synthesis of product **7** has been proposed in Scheme 4. At first, oxidation of compound **3** by periodic acid leads to intermediate **8**. This intermediate can convert to desired compound **7** through two pathways. In path A, compound **8** was hydrolysed to benzoic acid **9** and product **7** is formed *via* intramolecular cyclization. In path B, intramolecular intermediate **8** lead to intermediate **10** that was hydrolysed to intermediate **11**. Finally, intramolecular esterification of intermediate **11** lead to desired product **7**.

Experimental

All chemicals were purchased from Merck or Aldrich and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were recorded as

KBr pellets on FT-IR spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained using a Bruker DRX-400 AVANCE spectrometer. All NMR spectra were determined in DMSO-d_6. Chemical shifts are reported in parts per million (δ) downfield from an internal tetramethylsilane reference. Coupling constants (J values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), m (multiplet). Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 or 70 eV.

Scheme 4. Proposed mechanism for the compound **7**



General procedure for the synthesis of compound 3

A solution of salicylaldeyde (1 mmol) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (1 mmol) in EtOH (5 ml) were magnetically stirred in the presence of triethylamine (0.1 mmol) for 1 h under reflux. Then benzylamine (1 mmol) was added to the reaction mixture and the solution was stirred for 1 h under reflux. After this time, ninhydrin (1 mmol) was added to the mixture at room temperature and the solution stirred for 2 h. After completion of the reaction monitored by TLC, a dark solution has been achieved. The solvent was evaporated and residue recrystallized from ethyl acetate to give pure product 3**a**.

(3a*R*,8b*R*)-1-Benzyl-3a,8b-dihydroxy-2-methyl-3-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one(**3a**): Pale yellow powder, m.p = 157 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.16 (s, 3H, CH_3), 4.99 (d, $^2J_{HH}$ = 17.2 Hz, 1H, CH_2), 5.22 (d, $^2J_{HH}$ = 17.2 Hz, 1H, CH_2), 6.05 (s, 1H, OH), 7.22 (s, 1H, OH), 7.25 (d, $^3J_{HH}$ = 7.2 Hz, 2H, 2 CH_{meta} of Ph), 7.27 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH_{para} of Ph), 7.33 (d, $^3J_{HH}$ = 7.2 Hz, 2H, 2 CH_{ortho} of Ph), 7.39 (t, $^3J_{HH}$ = 8.0 Hz, 1H, CH of Ar), 7.46 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH of Ar), 7.59 (t, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.64 (td, $^3J_{HH}$ = 8.0 Hz,$^4J_{HH}$ = 2.2 Hz, 1H, CH of Ar), 7.69 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.72 (t, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.73 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.82 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.89 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ =14.5, 45.0, 83.9,95.0, 105.8, 116.1, 119.0, 123.3, 124.3, 125.0, 126.7, 127.0, 128.4, 128.7, 130.0, 130.5, 131.4, 134.7, 135.7, 137.8, 138.5, 147.9, 153.2, 158.5, 164.0, 184.3, 198.9 ppm; IR (KBr, cm^{-1}):3412 (2 OH), 1721 (3 C=O), 1606, 1478, and 1414 (Ar), 1357 and 1184 (C-O);MS (EI, 70 eV) *m/z* (%) =319 (5), 190 (5), 173 (12), 146 (66), 132 (37), 104 (100), 91 (74), 76 (97), 50 (38); Anal. calcd. for $C_{29}H_{21}NO_6$: C, 72.64; H, 4.41; N, 2.92%. Found: C, 72.55; H, 4.47; N, 2.88%. Crystal data for **3a** $C_{31}H_{21}N_2O_6$ (CCDC 935936): M_W = 517.50, monoclinic, space group C2/c, a = 25.2650(13) Å, b = 14.1121(10) Å, c = 14.5519(9) Å, α = 90 β = 92.961(5), γ = 90, V = 5181.4(6) Å^3, Z = 8, Dc = 1.327 mg/m^3, F (000) = 2152, crystal dimension 0.42×0.29×0.26 mm, radiation, Mo Kα (λ = 0.71073Å), 2.8≤2θ≤25.0, intensity data were collected at 295(2) K with a Bruker APEX area-detector diffractometer, and employing ω/2θ scanning technique, in the range of -25≤h≤30, -16≤k≤12, -17≤l≤14; the structure was solved by a direct method, all non-hydrogen atoms were positioned and anisotropic thermal parameters refined from 3149 observed reflections with R (into) = 0.1408 by a full-matrix least-squares technique converged to R = 0.1076 and Raw = 0.2509 [I>2sigma(I)].

(3a*R*,8b*R*)-1-(4-Chlorobenzyl)-3a,8b-dihydroxy-2-methyl-3-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3b**): Pale yellow powder, m.p = 160 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.17 (s, 3H, CH_3), 4.99 (d,$^2J_{HH}$ = 16.8 Hz, 1H, CH_2), 5.21 (d, $^2J_{HH}$ = 16.8 Hz, 1H, CH_2), 6.04 (s, 1H, OH), 7.25 (s, 1H, OH), 7.28 (d, $^3J_{HH}$ = 8.8 Hz, 2H, 2 CH of Ar), 7.37-7.42 (m, 3H, 3 CH of Ar), 7.46 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH of Ar), 7.60 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.64 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.68 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.72-7.74 (m, 2H, 2 CH of Ar), 7.83 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.88 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 14.4, 44.4, 83.9, 95.0, 105.9, 116.1, 119.0, 123.3, 124.3, 125.0, 128.3, 128.6, 128.7, 130.0, 130.5, 131.4, 131.6, 134.7, 135.7, 137.0, 138.5, 147.8, 153.2, 158.4, 163.8, 184.4, 198.2 ppm; IR (KBr, cm^{-1}): 3417 (2 OH), 1720 (3 C=O), 1607, 1480, and 1406 (Ar), 1189 (C-O); MS (EI, 70 eV) *m/z* (%) =353 (11), 180 (38), 146 (45), 125 (100), 104 (51), 89 (47), 77 (41), 63 (18); Anal. calcd. for $C_{29}H_{20}ClNO_6$: C, 67.78; H, 3.92; N, 2.73%. Found: C, 67.81; H, 3.98; N, 2.64%.

(3a*R*,8b*R*)-3a,8b-Dihydroxy-2-methyl-1-(4-methylbenzyl)-3-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-,3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3c**): Pale yellow powder, m.p = 162 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.16 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 4.94 (d, $^2J_{HH}$ = 16.8 Hz, 1H, CH_2), 5.18 (d, $^2J_{HH}$ = 16.8 Hz, 1H, CH_2), 6.01 (s, 1H, OH), 7.11-7.16 (m, 4H, 4 CH of Ar), 7.20 (s, 1H, OH), 7.38 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.46 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH of Ar), 7.59 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.64 (td, $^3J_{HH}$ = 8.0 Hz,$^4J_{HH}$ = 1.6 Hz, 1H, CH of Ar), 7.68 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.70-7.73 (m, 2H, 2 CH of Ar),

7.80 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.88 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ =14.5, 20.6, 44.8, 83.9, 95.0, 105.7, 116.0, 119.0, 123.2, 124.3, 125.0, 126.7, 128.7, 129.0, 130.1, 130.4, 131.4, 134.7, 135.7, 136.1, 138.5, 147.8, 147.9, 153.2, 158.5, 164.0, 184.3, 198.8 ppm; IR (KBr, cm^{-1}):3424 (2 OH), 1720 (3 C=O), 1609, 1563 and 1476 (Ar), 1188 (C-O); MS (EI, 70 eV) *m/z* (%) =333 (14), 160 (72), 132 (13), 105 (100), 76 (25), 50 (10). Anal. calcd. for $C_{30}H_{23}NO_6$: C, 73.01; H, 4.70; N, 2.84%. Found: C, 73.18; H, 4.78; N, 2.87%.

(3a*R*,8b*R*)-3a,8b-Dihydroxy-1-(4-methoxybenzyl)-2-methyl-3-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3d**): Pale yellow powder, m.p = 154-156 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ=2.17 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 4.90 (d,$^2J_{HH}$ = 16.8 Hz,1H, CH_2), 5.15 (d, $^2J_{HH}$ = 16.8 Hz, 1H, CH_2), 6.01 (s, 1H, OH), 6.90 (d, $^3J_{HH}$ = 8.8 Hz, 2H, 2 CH of Ar), 7.20 (d, $^3J_{HH}$ = 8.8 Hz, 2H, 2 CH of Ar), 7.21 (s, 1H, OH), 7.38 (t, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.46 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH of Ar), 7.60 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.64 (td, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.6 Hz, 1H, CH of Ar), 7.68 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.72 (dd, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.6 Hz, 1H, CH of Ar), 7.74 (td, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz, 1H, CH of Ar), 7.82 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.88 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ =14.5, 44.6, 55.0, 83.9, 95.0, 105.7, 113.8, 116.0, 119.0, 123.2, 124.3, 125.0, 128.1, 128.7, 129.5, 130.1, 130.4,131.4, 134.7, 135.7, 138.5, 147.9, 153.2, 158.3, 158.5, 164.0, 184.2, 198.9 ppm; IR (KBr, cm^{-1}): 3389 (2 OH), 1719 (3 C=O), 1606, 1481, and 1409 (Ar), 1350, 1243 and 1182 (C-O); MS (EI, 70 eV) *m/z* (%) = 509 (M$^+$, 1), 349 (55), 176 (79), 135 (43), 121 (100), 104 (42), 83 (98), 50 (21);Anal. calcd. for $C_{30}H_{23}NO_7$: C, 70.72; H, 4.55; N, 2.75%. Found: C, 70.76; H, 4.47; N, 2.83%.

(3a*R*,8b*R*)-3a,8b-Dihydroxy-1-(4-methoxybenzyl)-2-methyl-3-[(6-nitro-2-oxo-2*H*-chromen-3-yl)carbonyl]-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3e**): Beige powder, m.p = 185 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.19 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 4.92 (d,$^2J_{HH}$ = 16.4 Hz, 1H, CH_2), 5.15 (d, $^2J_{HH}$ = 16.4 Hz,1H, CH_2), 6.06 (s, 1H, OH), 6.90 (d, $^3J_{HH}$ = 8.0 Hz, 2H, 2 CH of Ar), 7.19 (d, $^3J_{HH}$ = 8.0 Hz, 2H, 2 CH of Ar), 7.29 (s, 1H, OH), 7.60 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.69 (d, $^3J_{HH}$ = 8.8 Hz, 1H, CH of Ar), 7.72 (d, $^3J_{HH}$ = 8.8 Hz, 1H, CH of Ar), 7.75 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.83 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH^8 of chromene), 8.05 (s, 1H, CH^4 of chromene), 8.45 (d, $^3J_{HH}$ = 8.0 Hz, 1H, CH^7 of chromene), 8.74 (s, 1H, CH^5 of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 14.6, 44.6, 55.0, 83.8, 95.2, 105.5, 113.8, 117.6, 119.4, 123.3, 124.4, 125.1, 126.1, 128.1, 129.4, 130.5, 131.3, 134.6, 135.8, 137.4, 143.6, 147.9, 156.9, 157.5, 158.3, 164.4, 183.1, 199.2 ppm; IR (KBr, cm^{-1}): 3437 (2 OH), 1732 (3 C=O), 1616, and 1413 (Ar), 1509 and 1346 (NO_2) 1350, 1247 and 1183 (C-O); MS (EI, 70 eV) *m/z* (%) = 275 (11), 218 (47), 191 (12), 172 (20), 132 (34), 104 (100), 76 (77), 50 (28); Anal. calcd. for $C_{30}H_{22}N_2O_9$: C, 64.98; H, 4.00; N, 5.05%. Found: C, 65.09; H, 3.91; N, 5.14%.

(3a*R*,8b*R*)-1-Benzyl-3a,8b-dihydroxy-3-[(8-methoxy-2-oxo-2*H*-chromen-3-yl)carbonyl]-2-methyl-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3f**): Yellow powder, m.p = 179-181 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.16 (s, 3H, CH_3), 3.96 (s, 3H, OCH_3), 4.98 (d,$^2J_{HH}$ = 17.0 Hz,1H, CH_2), 5.22 (d, $^2J_{HH}$ = 17.0 Hz, 1H, CH_2), 6.00 (s, 1H, OH), 7.21 (s, 1H, OH), 7.24-7.29 (m, 4H, 4 CH of Ar), 7.32-7.36 (m, 4H, 4 CH of Ar), 7.59 (t, $^3J_{HH}$= 7.6 Hz, 1H, CH of Ar), 7.68 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.72 (td, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.2 Hz, 1H, CH of Ar), 7.81 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH of Ar), 7.85 (s, 1H, CH^4 of chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 14.5, 45.0, 56.0, 83.9, 95.0, 105.8, 113.6, 119.5, 119.9, 123.2, 124.2, 125.0, 126.7, 127.0, 128.4, 130.2, 130.5, 134.7, 135.7, 137.8, 138.7, 142.5, 146.4, 147.9, 158.2, 163.9, 184.3, 200.0 ppm; IR (KBr, cm^{-1}): 3337 (2 OH), 1721 (3 C=O), 1608, and 1478 (Ar), 1271, 1181 and 1099 (C-O); MS (EI, 70 eV) *m/z* (%) = 242 (5), 203 (6), 176 (15), 146 (65), 121 (42), 105 (47), 91 (100), 76 (46), 51 (31). Anal. calcd. for $C_{30}H_{23}NO_7$: C, 70.72; H, 4.55; N, 2.75%. Found: C, 70.81; H, 4.43; N, 2.86%.

(3a*R*,8b*R*)-1-(4-Chlorobenzyl)-3a,8b-dihydroxy-3-[(8-methoxy-2-oxo-2*H*-chromen-3-yl)carbonyl]-2-methyl-3a,8b-dihydroindeno[1,2-*b*]pyrrol-4(1*H*)-one (**3g**): Yellow powder, m.p = 181-184 °C (dec). ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.17 (s, 3H, CH_3), 3.96 (s, 3H, OCH_3), 4.99 (d,$^2J_{HH}$ = 17.2 Hz,1H, CH_2), 5.21 (d,$^2J_{HH}$ = 17.2 Hz,1H, CH_2), 6.02 (s, 1H, OH), 7.25 (s, 1H, OH), 7.27-7.32 (m, 5H, 5 CH of Ar), 7.41 (d, $^3J_{HH}$ = 8.4 Hz, 2H, 2CH of Ar), 7.60 (t, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.68 (d, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.73 (t, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.84 (d, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.85 (s, 1H, CH^4 of chromene) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ =14.4, 44.4, 56.0, 83.9, 95.0, 106.0, 113.6, 119.5, 119.9, 123.3, 124.2, 125.0, 128.3, 128.6, 130.2, 130.5, 131.6, 134.7, 135.7, 137.0, 138.7, 142.5, 146.4, 147.8, 158.2, 163.8, 184.4, 198.8 ppm; IR (KBr, cm^{-1}): 3463 and 3244 (2 OH), 1705 (3 C=O), 1604, 1483 and 1407 (Ar), 1247, 1195 and 1102 (C-O); MS (EI, 70 eV) *m/z* (%) = 260 (40), 243 (11), 220 (21), 203 (83), 180 (37), 148 (18), 125 (80), 104 (99), 76 (100), 50 (61). Anal. calcd. for $C_{30}H_{22}ClNO_7$: C, 66.24; H, 4.07; N, 2.57%. Found: C, 66.12; H, 4.02; N, 2.65%.

General procedure for the synthesis of compound 7

To a solution of compound **3** (1 mmol) in EtOH (5 mL) periodic acid (1 mmol) was added, and the solution was stirred for 2 h at r.t. Then, the precipitate was filtered and was washed with acetone (4 ml) to afford the pure product **7**.

1'-Benzyl-5'-methyl-4'-(2-oxo-2*H*-chromene-3-carbonyl)-3*H*-spiro[isobenzofuran-1,2'-pyrrole]-3,3'(1'*H*)-dione (**7a**): White powder, m.p = 247-248 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.88 (s, 3H, CH_3), 4.54 (AB system,$^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 4.81 (AB system, $^2J_{HH}$ = 16.2 Hz, 1H, CH_2), 7.13 (d, $^3J_{HH}$ = 5.1 Hz, 2H, 2 CH of Ar), 7.14-7.34 (m, 3H, 3 CH of Ar), 7.36 (d, $^3J_{HH}$ = 7.7 Hz, 3H, 3 CH of Ar), 7.58 (d, $^3J_{HH}$ = 9.1 Hz, 1H, CH of Ar), 7.63 (t, $^3J_{HH}$ = 9.3 Hz, 1H, CH of Ar), 7.71 (t, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.77 (d, $^3J_{HH}$ = 6.5 Hz, 1H, CH of Ar), 7.91 (d, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 8.06 (s, 1H, CH of Chromene)

ppm; ^{13}C NMR (DMSO-d_6, 75.0 MHz): δ = 16.0, 46.5, 94.3, 108.1, 116.2, 118.4, 123.0, 124.8, 125.7, 126.0, 127.3, 127.7, 128.6, 129.4, 130.0, 131.8, 132.9, 135.1, 135.5, 141.2, 141.4, 153.5, 158.0, 167.1, 182.9, 186.7, 188.3 ppm; IR (KBr, cm^{-1}): 1795 (CO_2), 1721 (CO_2), 1690 (2 C=O), 1634 and 1502 (Ar), 1191 and 1079 (C-O); MS (EI, 70 eV): *m/z* (%) = 477 (M^+, 1), 254 (19), 173 (8), 146 (9), 127 (100), 104 (22), 91 (50), 76 (24), 50 (17); Anal. calcd. for $C_{29}H_{19}NO_6$: C, 72.95; H, 4.01; N, 2.93%. Found: C, 72.87; H, 4.06; N, 2.97%. Crystal data for **7a** $C_{29}H_{19}N_1O_6$ (CCDC 1033422): M_W = 477.5, a = 11.2256(2) Å, b = 12.7218(3) Å, c = 16.4454(3) Å, α =90, β = 103.055(2), γ = 90, V = 2287.86(8) Å^3, Z = 4, Dc = 1.3862 mg/m^3, F (000) = 992, Cu K\a (λ = 1.54184 Å), 4.35≤2θ≤67.13, intensity data were collected at 120 K with a Xcalibur, Atlas, Gemini ultra-area-detector diffractometer, and employing ω/2θ scanning technique,, and employing ω/2θ scanning technique, in the range of -13≤h≤13, -13≤k≤14, -19≤l≤19; the structure was solved by a direct method, all non-hydrogen atoms were positioned and anisotropic thermal parameters refined from 4060 observed reflections with *R* (int) = 0.0317 by a full-matrix least-squares technique converged to *R* = 0.0348 and wR_2 = 0.1070 [I>2sigma(I)].

1'-(4-Chlorobenzyl)-5'-methyl-4'-(2-oxo-2*H*-chromene-3-carbonyl)-3*H*-spiro[isobenzofuran-1,2'-pyrrole]-3,3'(1'*H*)-dione (**7b**): White powder, m.p = 230-232 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.89 (s, 3H, CH_3), 4.57 (AB system, $^2J_{HH}$ = 13.7 Hz,1H, CH_2), 4.80 (AB system,$^2J_{HH}$ = 13.7 Hz,1H, CH_2), 7.07-7.24 (m, 3H, 3 CH of Ar), 7.27-7.42 (m, 4H, 4 CH of Ar), 7.61 (d, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.69-7.77 (m, 3H, 3 CH of Ar), 7.92 (d, $^3J_{HH}$ = 6.5 Hz, 1H, CH of Ar), 8.06 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 75.0 MHz): δ = 15.9, 45.7, 94.2, 108.2, 116.1, 118.4, 123.0, 124.7, 125.7, 126.0, 128.5, 129.2, 129.4, 129.9, 131.8, 132.3, 132.8, 134.1, 135.4, 141.1, 141.4, 153.5, 157.9, 167.0, 182.9, 186.6, 188.2 ppm; IR (KBr, cm^{-1}):1785 (CO_2), 1713 (3 C=O), 1614 and 1512 (Ar), 1193 and 1081 (C-O); MS (EI, 70 eV): *m/z* (%) = 511 (M^+, 1), 368 (29), 242 (13), 214 (58), 186 (83), 173 (48), 147 (18), 125 (100), 104 (35), 89 (51), 76 (31), 50 (4); Anal. calcd. for $C_{29}H_{18}ClNO_6$: C, 68.04; H, 3.54; N, 2.74%. Found: C, 67.97; H, 3.50; N, 2.81%.

5'-Methyl-1'-(4-methylbenzyl)-4'-(2-oxo-2*H*-chromene-3-carbonyl)-3*H*-spiro[isobenzofuran-1,2'-pyrrole]-3,3'(1'*H*)-dione (**7c**): White powder, m.p = 264-266 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.20 (s, 3H, CH_3), 2.87 (s, 3H, CH_3), 4.45 (AB system, $^2J_{HH}$ = 14.1 Hz,1H, CH_2), 4.74 (AB system, $^2J_{HH}$ = 13.7 Hz, 1H, CH_2), 6.53-7.25 (s, 4H, 4 CH of Ar), 7.33-7.40 (m, 3H, 3 CH of Ar), 7.58-7.88 (m, 5H, 5 CH of Ar), 8.04 (s, 1H, CH of Chromene) ppm; ^{13}C NMR (DMSO-d_6, 75.0 MHz): δ = 15.9, 20.6, 46.3, 94.3, 108.1, 116.1, 118.3, 122.9, 124.7, 125.6, 126.0, 127.2, 129.1, 129.3, 130.0, 131.7, 131.9, 132.8, 135.4, 136.9, 141.3, 141.4, 153.5, 158.0, 167.0, 182.9, 186.5, 188.2 ppm; IR (KBr, cm^{-1}): 1792 (CO_2), 1705 (3 C=O), 1616 and 1508 (Ar), 1200 and 1079 (C-O); MS (EI, 70 eV): *m/z* (%) = 491 (M^+, 2), 368 (16), 254 (26), 173 (100), 127 (40), 105 (84), 77 (16); Anal. Calcd. for $C_{30}H_{21}NO_6$: C, 73.31; H, 4.31; N, 2.85%. Found: C, 73.36; H, 4.22; N, 2.80%.

1'-Benzyl-4'-(8-methoxy-2-oxo-2*H*-chromene-3-carbonyl)-5'-methyl-3*H*-spiro[isobenzofuran-1,2'-pyrrole]-3,3'(1'*H*)-dione (**7f**): White powder, m.p = 250-251 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.86 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 4.54 (AB system, $^2J_{HH}$ = 16.6 Hz,1H, CH_2), 4.80 (AB system,$^2J_{HH}$ = 16.6Hz, 1H, CH_2), 7.13 (d, $^3J_{HH}$ = 6.0 Hz, 2H, 2 CH of Ar), 7.25-7.31 (m, 6H, 6 CH of Ar), 7.57 (d, $^3J_{HH}$ = 7.4 Hz, 1H, CH of Ar), 7.69 (t, $^3J_{HH}$ = 7.2 Hz, 1H, CH of Ar), 7.76 (t, $^3J_{HH}$ = 7.1 Hz, 1H, CH of Ar), 7.91 (d, $^3J_{HH}$ = 7.1 Hz, 1H, CH of Ar), 8.03 (s, 1H, CH[4] of chromene)ppm; ^{13}C NMR (DMSO-d_6, 75.0 MHz): δ = 15.9, 46.4, 56.1,94.3, 108.1, 115.0, 118.9, 120.4, 122.9, 124.6, 125.6, 126.0, 127.2, 127.7, 128.6, 130.0, 131.8, 135.0, 135.4, 141.2, 141.6, 142.8, 146.3, 157.7, 167.0, 182.9, 186.6, 188.2 ppm; IR (KBr, cm^{-1}):1794 (CO_2), 1721 (3 C=O), 1607 and 1496 (Ar), 1194 and 1095 (C-O); MS (EI, 70 eV): *m/z* (%) = 507 (M^+, 1), 279 (16), 183 (18), 167 (57), 149 (100), 111 (22), 69 (57), 55 (32). Anal. calcd. for $C_{30}H_{21}NO_7$: C, 71.00; H, 4.17; N, 2.76%. Found: C, 70.95; H, 4.06; N, 2.83%.

Conclusions

In summary, we have disclosed a novel method for the synthesis of products **3** and **7** by a four-component sequential reaction and following oxidative cleavage reaction. This protocol has some advantages such as, easy performance, easy purification, good yields, use of simple reactant and simple reaction conditions (no metal catalysts, no inert atmosphere and or no dry solvent). The products that described in this article can have biological activities due to their important heterocycle moieties. According to our knowledge, this class of coumarins is reported first time and there are no other efficient methods for their synthesis. Due to the importance of the coumarin skeleton, synthetic and biological applications of compounds **3** and **7** can be considered in the near future.

Notes and references

1 R. D. H. Murray, Mendez, Brown, J.; S. A. The Natural coumarins: Occurrence, chemistry and biochemistry, John Wiley & Sons Ltd., New York, 1982, p. 21.

2 A. K., Okamoto, A. C. Gaudio, A. D. S. Marques, Y. Takahata, *J. Mol. Struct.: Theochem* 2005, **725**, 231.

3 R. O'Kennedy, R. Zhorenes, Coumarins: Biology, Applications and mode of action; John Wiley and Sons: Chichester, 1997.

4 M. Zabradnik, The production and application of fluorescent brightening agents; John Wiley & Sons; New York, 1992.

5 A. Kamal, S. F. Adil, J. R. Tamboli, B. Siddardha, U. S. N. Murthy, *Lett. Drug Des. Discovery* 2009, **6**, 201.

6 (a) Y. K. Tyagi, A. Kumar, H. G. Raj, P. Vohra, G. Gupta, R. Kumari, P. Kumar, R. K. Gupta, *Eur. J. Med. Chem*. 2005, **40**, 413; (b) C. A. Kontogiorgis, K. Savvoglou, D. J. Hadjipavlou-Litina, *J. Enzyme Inhib. Med. Chem*. 2006, **21**, 21.

7 (a) D. E.; Zembower, S.; Liao, M. T.; Flavin, Z. Q.; Xu, T. L.; Stup, R. W.; Buckheit, A.; Khilevich, A. A.; Mar, A. K. Sheinkman, *J. Med. Chem.* 1997, **40**, 1005; (b) N. A. Al–Masoudi, I. A. AlMasoudi, I. A. I. Ali, Y. A. Al-Soud, B. Saeed. P. L. Colla, *Acta Pharm.* 2006, **56**, 175.

8 G. Cravotto, G. M. Nano, G. Palmisano, S. Tagliapietra, *Tetrahedron: Asymmetry* 2001, **12**, 707.

9 (a) H. H. Sayed, A. H. Shamroukh, A. E. Rashad, *Acta Pharm.* 2006, **56**, 231; (b) S. Sardari, Y. Mori, K. Horita, R. G. Micetich, S. Nishibe, M. Daneshtalab, *Bioorg. Med. Chem*. 1999, **7**, 1933.

10 C. A.; Kontogiorgis, D. J. Hadjipavlou-Litina, *J. Med. Chem*. 2005, **48**, 6400.

11 F. Leonetti, A. Favia, A. Rao, R. Aliano, A. Paluszcak, R. W. Hartmann, A. Carotti, *J. Med. Chem*. 2004, **47**, 6792.

12 L. M. Kabeya, A. A. de Marchi, A. Kanashiro, N. P. Lopes, C. H. T. P. da Silva, M. T. Pupo, Y. M. Lucisano-Valima, *Bioorg. Med. Chem*. 2007, **15**, 1516.

13 L. Piazzi, A. Cavalli, F. Colizzi, F. Belluti, M. Bartolini, F. Mancini, M. Recanatini, V. Andrisano, A. Rampa, *Bioorg. Med. Chem. Lett*. 2008, **18**, 423.

14 K. Harada, H. Kubo, Y. Tomigahara, K. Nishioka, J. Takahashi, M. Momose, S. Inoue, A. Kojima, *Bioorg. Med. Chem. Lett.* 2010, **20**, 272.

15 S. Ravichandran, *Synth. Commun*. 2001, **31**, 1233.

16 (a) Q. Wang, M. G. Finn, *Org. Lett.* 2000, **2**, 4063; (b) N. A. Petasis, A. N. Butkevich, *J. Organomet. Chem.* 2009, **694**, 1747.

17 N. Majumdar, K. A. Korthals, W. D. Wulff, *J. Am. Chem. Soc.* 2012, **134**, 1357.

18 S. Kim, D. Kang, C.-H. Lee, P. H. Lee, *J. Org. Chem*. 2012, **77**, 6530.

19 B. Schmidt, S. Krehl, A. Kelling, U. Schilde, *J. Org. Chem*. 2012, **77**, 2360.

20 D. Tejedor, L. Cotos, F. García-Tellado, *J. Org. Chem*. 2013, **78**, 8853.

21 (a) D. R. Gauta, J. Protopappas, K. C. Fylaktakidou, K. E. Litinas, D. N. Nicolaides, C. A. Tsoleridis, *Tetrahedron Lett*. 2009, **50**, 448; (b) K. C. Majumdar, S. Samanta, I. Ansary, B. Roy, *RSC Advances* 2012, **2**, 2137; (c) M. Roussaki, C. A. Kontogiorgis, D. J. Hadjipavlou-Litina, S. Hamilakis, A. Detsi, *Bioorg. Med. Chem. Lett*.2010, **20**, 3889; (d) A. R. Katritzky, T. S. Ibrahim, S. R. Tala, N. E. Abo-Dya, Z. K. Abdel-Samii, S. A. El-Feky, *Synthesis* 2011, **9**, 1494; (e) V. S. Moshkin, V. Y. Sosnovskikh, G. V. Röschenthaler, *Tetrahedron Lett*. 2012, **53**, 3568; (f) G. Pal, S. Paul, A. R. Das, *Synthesis* 2013, **45**, 1191.

22 C. H. Heathcock, S. L. Graham, M. C. Pirrung, F. Plavac, C. T. White, Spirocyclic Systems In The Total Synthesis of Natural Products; Simon, J., Ed.; John Wiley & Sons: New York, 1983; Vol. 5, p 264.

23 (a) R. A. Jones, G. P. Bean, The Chemistry of Pyrroles; Academic Press: London, 1977. (b) B. Sadek, C. Limban, C. E. Stecoza, S. Elz, *Sci. Pharm*. 2011, **79**, 749; (c) F. F. Ma, Y. Gao, H. L. Qiao, X. J. Hu, J. B. Chang, *J. Thromb. Thrombolys*. 2012, **33**, 64; (d) S. L. Zhang, Y. J. Liu, Y. F. Zhao, Q. T. Guo, P. Gong, *Chin. Chem. Lett*. 2010, **21**, 1071.

24 (a) E. D. Olmo, M. G. Armas, M. I. Ybarra, J. L. López, P. Oporto, A. Giménez, E. Deharo, A. S. Feliciano, *Bioorg. Med. Chem. Lett.* 2003, **13**, 2769; (b) A. E. Kümmerle, M. M. Vieira, M. Schmitt, A. L. P. Miranda, C. A. M. Fraga, J. J. Bourguignon, E. J. Barreiro, *Bioorg. Med. Chem. Lett.* 2009, **19**, 4963; (c) P. Manivel, F. N. Khan, V. R. Hatwar, *Phosphorus, Sulfur Silicon Relat. Elem*. 2010, **185**, 1932; (d) A. R. Ramesha, A. K. Roy, *Synth*. *Commun*. 2001, **31**, 2419.

25 (a) M. R. Mohammadizadeh, N. Firoozi, R. Aradeh, *Helv. Chim. Acta* 2011, **94**, 410; (b) Y. Fan, S. Liu, N. Chen, X. Shao, X. Xu, Z. Li, *Synlett* 2015, **26**, 393; (c) G. H. Mahdavinia, M. R. Mohammadizadeh, N. Ariapour, M. Alborz, *Tetrahedron Lett*. 2014, **55**, 1967; (d) M. R. Mohammadizadeh, M. Bahramzadeh, S. Zainabakhtoon Taghavi, *Tetrahedron Lett*. 2010, **51**, 5807; (e) Y. Malpani, R. Achary, S. Y. Kim, H. C. Jeong, P. Kim, S. B. Han, M. Kim, C. K. Lee, J. N. Kim, Y. S. Jung, *Eur. J. Med. Chem*. 2013, **62**, 534.

26 A. Alizadeh, R. Ghanbaripour, *Helv. Chim. Acta* 2013, **96**, 473.

27 (a) M. Rahman, A. Sarkar, M. Ghosh, A. Majee, A. Hajra, *Tetrahedron Lett*. 2014, **55**, 235; (b) T. Amanpour, K. Zangger, F. Belaj, A. Bazgir, D. Dallinger, C. O. Kappe, *Tetrahedron* 2015, **71**, 7159; (c) Z. Lu, J. Xiao, D. Wang, Y. Li, *Asian J. Org. Chem*. 2015, **4**, 381; (d) A. Alizadeh, M. Hossein Abadi, R. Ghanbaripour, *Synlett* 2014, **25**, 1705; (e) A. Alizadeh, R. Ghanbaripour, S. W. Ng, *Helv. Chim. Acta* 2015, **98**, 663; (f) S. Sarkar, A. T. Khan, *Chem. Commun*. 2015, **51**, 12673; (g) L. Wang, Z. L. Ren, M. W. Ding, *J. Org. Chem*. 2015, **80**, 641; (h) W. M. Shu, K. L. Zheng, J. R. Ma, H. Y. Sun, M. Wang, A. X. Wu, *Org. Lett*. 2015, **17**, 1914; (i) D. J. Jung, H. J. Jeon, J. H. Lee, S. G. Lee, *Org. Lett*. 2015, **17**, 3498.

28 (a) A. Alizadeh, R. Ghanbaripour, L. G. Zhu, *Synlett* 2013, **24**, 2124; (b) A. Alizadeh, R. Ghanbaripour, L. G. Zhu, *Synlett* 2014, **25**, 1596; (c) A. Alizadeh, M. R. Ghanbaripour, *Synlett* 2014, **25**, 2777; (d) A. Alizadeh, R. Ghanbaripour, *Synth. Commun.* 2014, **44**, 1635; (e) A. Alizadeh, R. Ghanbaripour, L. G. Zhu, *Tetrahedron* 2014, **70**, 2048; (f) A. Alizadeh, R. Ghanbaripour, *Helv. Chim. Acta* 2014, **97**, 895.

29 (a) D. Q. Shi, Y. Zhou, S. F. Rong, *Synth. Commun*. 2009, **39**, 3500; (b) J. Svetlik, N. Pronayava, V. Hanus, *J. Heterocycl. Chem*. 2000, **37**, 395; (c) T. S. Shaikh, K. A. Undale, D. S. Gaikwad, D. M. *C.* Pore, *R. Chimie* 2011, **14**, 987; (d) O. S. Darwish, K. A.; Granum, Q. Tan, R. P. Hsung, *Tetrahedron Lett*. 2001, **42**, 3283; (e) O. Talhi, M. Makhloufi-Chebli, D. C. G. A. Pinto, M. Hamdi, A. M. S. Silva, *Synlett* 2013, **24**, 2559.

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