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ORIGINAL PAPER

Microwave assisted one pot synthesis of 7-substituted 2-(2-oxo-2*H*-chromen-3-yl)acetic acids as precursors of new anti-tumour compounds

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Perkin condensation with subsequent intramolecular lactonisation as one pot syntheses of 2-(2-oxo-2*H*-chromen-3-yl)acetic acids *VIIa–Xa* has been studied. The required acids *VIIa–Xa* were prepared as precursors of recently discovered compounds possessing antineoplastic activities. Syntheses of *VIIa–Xa* were carried out using *para* substituted 2-hydroxybenzaldehydes *II–VI*, succinic acid anhydride, sodium succinate under thermal or microwave conditions. Significant shortening of the reaction time under microwave irradiation was observed (18–50 min instead of 1.5–5 h of heating). Microwave assisted reactions proceeded more smoothly to give higher yield of the required products *VIIa–Xa* (31–61 %) compared to those under classical thermal conditions e.g. 21.8 % for *IXa* (Hurenkamp et al., 2007). Seven reaction by-products were isolated and determined as 2*H*,2′*H*-3,3′-bichromene-2,2′-diones *VIIb–Xb* and (*E*)-3-(2-hydroxystyryl)-2*H*-chromen-2-ones *VIIc–IXc*.

Keywords: microwave, coumarine, Perkin condensation, Perkin lactonisation, anti-cancer compounds, fluorescence

Introduction

Development of new antineoplastic compounds is highly required because of yearly increasing amount of cancer events (National Cancer Institute, 2010). Recently, several new compounds with the leading skeleton (*L*) have been prepared (Fig. 1). Their anticancer activities were determined on the sixty human tumour cell lines assay in NCI USA (GI_{50}: 10^{-6}–10^{-8} M) (NCI/NIH, 2010). The particular mechanism of their cytostatic influence is not yet known. Their structures and biological activities were described by Lácová & Boháč (2006). Skeleton (*L*) represents a conjugated system of two aromatic rings and three double bonds that allow studying the relationship between biological activities and electron distributions within the possible push–pull system. Structures and syntheses of new lead compounds (*L*) are depicted in Fig. 1.

The aim of this work was to find convenient and optimal conditions for the preparation and purification of *VIIa–Xa* and all reaction by-products.

Experimental

Resorcinol (*I*), 3-(*N*,*N*-dimethylamino)phenol (*II*) and $Zn(CN)_2$ were purchased from Sigma–Aldrich (Germany). Hexanes is a commercially available mixture of nonpolar solvents (light fraction of hydrocarbons from petrol), b.p. 45–65 °C. Condensation reactions were performed in a Microwave oven Sencor SMW5020 (USA), 800W, 2450 MHz, with power regulation. Solvents were dried and purified using conventional methods. DMF was dried by distillation from $CaH_2 \cdot POCl_3$, and distilled prior to use. All reactions were carried out under argon atmosphere. TLC was performed on Merck F_{254} silica gel precoated on alu-

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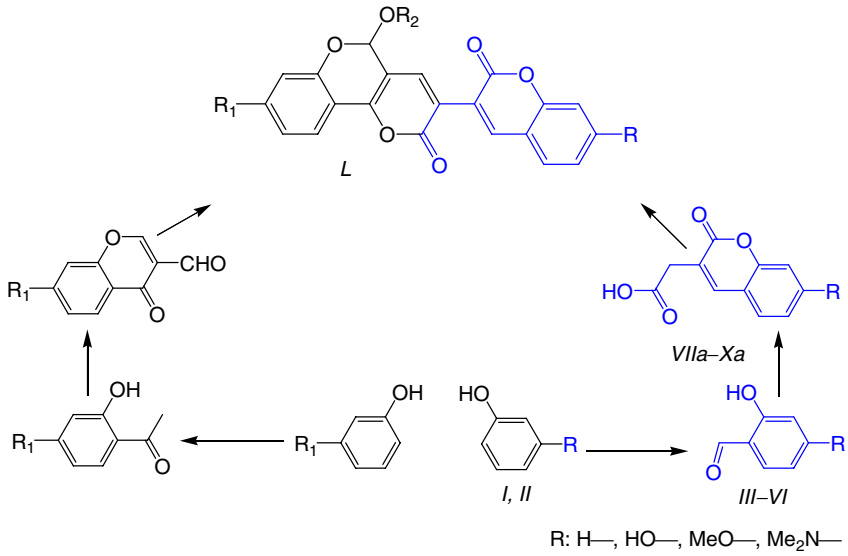

Fig. 1. Convergent synthesis of compounds *L* requiring the preparation of 2-(2-oxo-2*H*-chromen-3-yl)acetic acids *VIIa–Xa* from 3-substituted phenols. Optimal *meta* position of substituents R and R^1 was chosen for the best electronic influence on the possible push–pull system in *L*.

mina plates. For the spots detection, a UV lamp (254 nm) and I_2 vapours were used. Melting points (m.p.) were determined on a Kofler hot stage and are uncorrected. Simple distillations were performed on a Büchi KGR apparatus. FTIR spectra were recorded as solid samples on a FTIR-ART REACT IR 1000 (ASI Applied Systems, UK) instrument in the region of 650–4002 cm^{-1}. Elemental analyses (C, H, N) were obtained by a Carlo Erba Strumentazione Model 1106 analyzer (Italy). ^1H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini (USA) (300 MHz for ^1H or 75.4 MHz for ^{13}C) spectrometer in $CDCl_3$ or DMSO-d^6. Chemical shifts based on TMS and coupling constants (J) are in Hz. HETCOR, HMQC, COSY, or NOE techniques were used for exact spectral assignments. Compounds *VIIb–Xb* were not soluble enough even in warm DMSO and their ^{13}C NMR and FTIR spectra could not be recorded.

General procedure for preparation of VIIa–Xb

Synthesis of *VIIa–VIIc* by condensation of salicylaldehyde (*III*) with succinic acid anhydride was performed as follows. A mixture of salicylaldehyde *III* (2.30 g, 18.83 mmol), succinic acid anhydride (9.42 g, 94.13 mmol) and sodium succinate (4.06 g, 25.05 mmol) in absolute DMF (5.00 mL) was heated in a microwave oven at 250 W (9 × 2 min) until complete consumption of salicylaldehyde *III* (determined by TLC: SiO_2, hexanes : EtOAc, $\varphi_r = 0.5$, $R_F = 0.71$). Afterwards, the mixture was acidified with 10 % HCl (20 mL) and stirred at room temperature for 30 min to allow the hydrolysis of the excess succinic acid anhydride. Insoluble 2*H*,2′*H*-3,3′-bichromene-2,2′-dione (*VIIb*) was filtered off, washed with small amounts of H_2O, $CHCl_3$ and dried on air (371.4 mg, 1.28 mmol, 13.6 %). The water solution was extracted with $CHCl_3$ (6 × 20 mL). $CHCl_3$ was chosen as the solvent because it dissolves *VIIa* and *VIIc* but not the excess succinic acid. Combined $CHCl_3$ solution was extracted with saturated aqueous Na_2CO_3 (4 × 20 mL). The by-product *VIIc* was separated from the evaporated $CHCl_3$ organic layer and purified by flash chromatography (SiO_2, hexanes : EtOAc, $\varphi_r = 0.5$) (99.4 mg, 0.38 mmol, 4.0 %). The basic water phase was separated, acidified by 10 % HCl (30 mL) and extracted with EtOAc (3 × 70 mL). The combined ethyl acetate layer was dried over Na_2SO_4, filtered and evaporated on rotary evaporator. 2-(2-Oxo-2*H*-chromen-3-yl)acetic acid (*VIIa*) was obtained (2.35 g, 11.51 mmol, 61.2 %) as ochreous powder. Crude acid *VIIa* was purified by crystallisation from hot H_2O. The result was comparable to those presented in literature (60 % yield after 5 h at 185 °C (Ito, 1951) or 57 % after 1.5 h of reflux in $(Et)_3N$ (Bochkov et al., 2008)). 2-(2-Oxo-2*H*-chromen-3-yl)acetic acid (*VIIa*) is a yellow crystalline compound with m.p. of 154.0–158.0 °C (H_2O); 157.5 °C (Ito, 1951). 2*H*,2′*H*-3,3′-Bichromene-2,2′-dione (*VIIb*) is a pale yellow powder with m.p. of 319.0–323.0 °C; 315.0 °C (Dey & Sankaranarayanan, 1931). 3-(2-Hydroxystyryl)-2*H*-chromen-2-one (*VIIc*) is a yellow crystalline compound with m.p. of 208.0–213.0 °C (FLC); 207.0 °C (Dey & Sankaranarayanan, 1931).

The above procedure was used also for other starting aldehydes. The conditions and yields are shown in Table 1. Characterisation and spectral data of the newly prepared compounds are given in Tables 2 and 3, respectively.

Condensation of 2,4-dihydroxylbenzaldehyde (*IV*)

Table 1. Reaction conditions and obtained product yields for different starting aldehydes

Aldehyde	Succinic acid anhydride to $Na_2(OOCCH_2)_2$ mole ratio	Microwave		Product yield[b]/%			
		Power/W	Time/min		*a*	*b*	*c*
III[a]	5.00 : 1.33	250	9 × 2	*VII*	61	14	4
IV[c]	4.00 : 1.33	350	6 × 2	*VIII*	31	9	0.5
V[d]	4.00 : 1.33	350	10 × 3	*IX*	40	12	3
VI[e]	4.00 : 1.33	500	10 × 5	*X*	31	0.4	0

a) Only in this case 5 mL of DMF per 18.8 mmol of starting aldehyde *III* were used, other reactions were carried out under solvent free conditions; *b*) reactions were performed in scale from 3.0 mmol to 18.8 mmol of the starting aldehydes (corresponding to 0.5–2.3 g of the appropriate aldehydes); *c*) mixture was carefully melted by a hot melt gun just before microwave irradiation, crude solid product could be extracted by $CHCl_3$ in a Soxhlet apparatus overnight instead of the extraction using water solution, pre-purified product *VIIIa* was contaminated with succinic acid which was removed by an in situ conversion at 175 °C under HV to volatile succinic acid anhydride that sublimed off the mixture on a Büchi KGR apparatus. Crude solid material left after the sublimation was crystallised from the mixture of H_2O/EtOH; *d*) reaction mixture was melted by a hot melt gun before microwave irradiation; *e*) conversion of *VI* was not better even if higher excess of succinic acid anhydride or prolonged microwave irradiation were used. In such case more polymeric material was produced. Basic properties of product *X*a (containing Me_2N— group) had to be considered by its isolation and pH had to be carefully adjusted in the range of 5–6 for its successful precipitation from the water solution.

with succinic acid anhydride: The obtained products: 2-(7-Hydroxy-2-oxo-2*H*-chromen-3-yl)acetic acid (*VIIIa*) white crystalline compound. M.p. 217.0–220.0 °C (H_2O / EtOH). 7,7′-Dihydroxy-[3,3′]bichromenyl-2,2′-dione (*VIIIb*) ocherous powder. M.p. 296.0–298.0 °C (DMSO / H_2O). 18 % yield from 7-hydroxycoumarine by oxidative coupling with $FeCl_3$ at 50 °C within 2 h (Reisch & Zappel, 1992). 3-(2,4-Dihydroxystyryl)-7-hydroxy-2*H*-chromen-2-one (*VIIIc*) yellow crystalline compound, m.p. 250.0–252.5 °C (H_2O /EtOH).

Condensation of 2-hydroxy-4-methoxybenzaldehyde (*V*) with succinic acid anhydride was performed. Obtained products were: 2-(7-methoxy-2-oxo-2*H*-chromen-3-yl)acetic acid (*IXa*), ocherous crystalline compound with m.p. of 179.0–182.0 °C (decomposing) (H_2O/EtOH); 177.5–177.9 °C (H_2O/EtOH) (Hurenkamp et al., 2007), 7,7′-dimethoxy-[3,3′]bichromenyl-2,2′-dione (*IXb*), pale yellow powder with m.p. of 293–294 °C (DMSO) (Lele et al., 1961), and 3-(2-hydroxy-4-methoxystyryl)-7-methoxy-2*H*-chromen-2-one (*IXc*), yellow crystalline powder with m.p. of 250.0 °C (decomposing) (FLC).

Condensation of 4-(dimethylamino)-2-hydroxybenzaldehyde (*VI*) with succinic acid anhydride was done and products: 2-(7-*N*,*N*-dimethylamino-2-oxo-2*H*-chromen-3-yl)acetic acid (*Xa*), yellow crystalline compound with m.p. of 190.0–195.0 °C (acetone/H_2O), and 7,7′-*N*,*N*-dimethylamino-[3,3′]bichromenyl-2,2′-dione (*Xb*), pale yellow crystalline compound with m.p. of 230.0 °C (decomposing) (DMSO/H_2O), were obtained.

Results and discussion

One pot syntheses of 2-(2-oxo-2*H*-chromen-3-yl)-acetic acids *VIIa–Xa* starting from *para* substituted 2-hydroxybenzaldehydes *III–VI*, succinic acid anhydride, and sodium succinate carried out by microwave irradiation are described. It was observed that microwave assisted reactions proceeded more smoothly and they provided higher yields of the required products *VIIa–Xa* compared to those obtained by thermal syntheses. Significant shortening of the reaction time under microwave irradiation was recorded (18–50 min instead of 1.5–5 h under common heating). Convenient isolation of products *VIIa–Xa* by acid-base extraction is described. Structures of all observed by-products *VIIb–Xb* and *VIIc–IXc* were determined. By-products 2*H*,2′*H*-3,3′-bichromene-2,2′-diones *VIIb–Xb* were formed subsequently from *VIIa–Xa* by additional condensation with the appropriate aldehydes *III–VI* followed by dehydration of intermediates. Intermadiates 3,3′-bichromene-2,2′-diones *VIIb–Xb* were not soluble enough even in warm DMSO and therefore some of their spectra could not be recorded. Formation of (*E*)-3-(2-hydroxystyryl)-7-methyl-2*H*-chromen-2-ones *VIIc–IXc* was expected during high temperature decarboxylation of intermediates (Fig. 2).

para Substituted salicylaldehydes *IV–VI* were prepared from resorcinol (*I*) or 3-(dimethylamino)phenol (*II*). 2,4-Dihydroxybenzaldehyde (*IV*) was prepared in a 68 % yield by the Gattermann–Adams formylation from resorcinol (*I*), $Zn(CN)_2$ and HCl (g) (Fig. 3) (Adams & Levin, 1923) as the Vilsmeier–Haack formylation of *I* is less advantageous (Vilsmeier & Haack, 1927). In case of the latter, lower yield (50 %) and also *O*-formylated by-products were observed.

Selective monomethylation of 2,4-dihydroxybenzaldehyde (*IV*) by $KHCO_3$/MeI was used to synthesise 2-hydroxy-4-methoxybenzaldehyde (*V*) in a 60 % yield (Binnemans et al., 2000). The observed regioselectivity was explained by different ability of $KHCO_3$ to abstract protons from the two hydroxyl groups of *IV*. The hydroxy group in *para* position is more acidic compared to that in the *ortho* position. Product *V* was selectively isolated from the crude mixture by trituration in hexanes. Nonpolar hexanes did not solve the

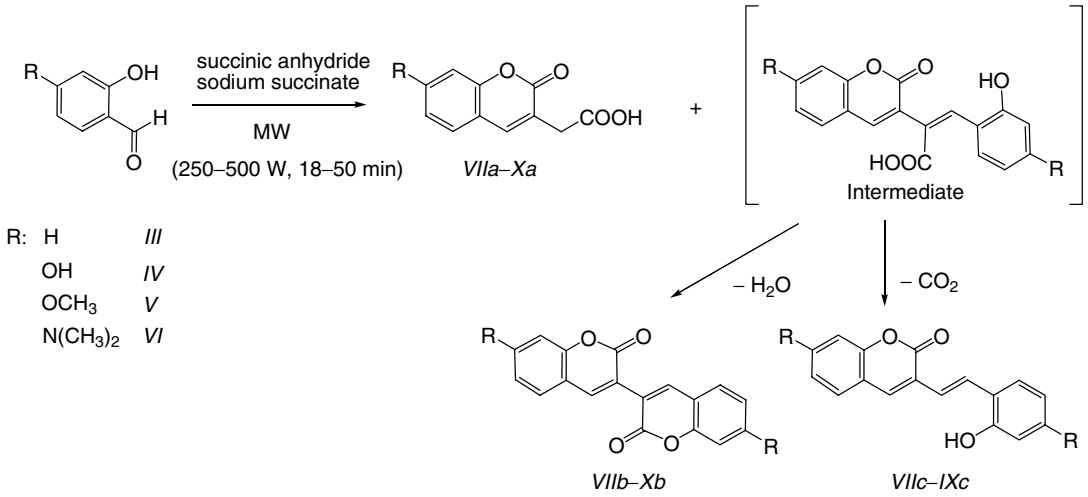

Fig. 2. Proposed mechanism for the formation of desired products *VIIa–Xa* and all observed reaction by-products *VIIb–Xb*, *VIIc–IXc* and their yields.

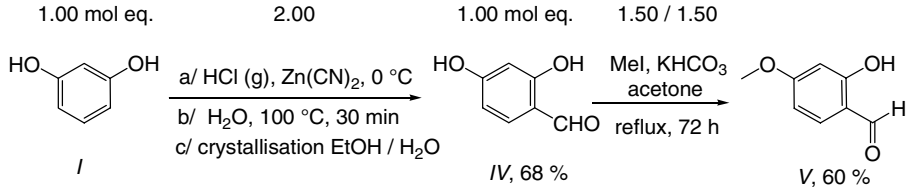

Fig. 3. Synthesis of 2,4-dihydroxybenzaldehyde (*IV*) under Adams conditions and 2-hydroxy-4-methoxybenzaldehyde (*V*) by methylation of *IV*.

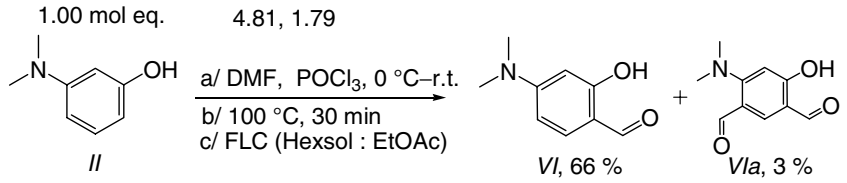

Fig. 4. Synthesis of 4-(dimethylamino)-2-hydroxybenzaldehyde (*VI*) and *VIa* under Vilsmeier–Haack conditions.

Table 2. Characterisation data of newly prepared compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield/%	M.p./°C
			C	H	N		
VIIIc	$C_{17}H_{12}O_5$	296.27	68.92 69.03	4.08 4.15	–	0.5	250.0–252.5
IXc	$C_{19}H_{16}O_5$	324.33	70.36 70.62	4.97 5.02	–	3	250.0[a]
Xa	$C_{13}H_{13}NO_4$	247.25	63.15 63.07	5.30 5.42	5.67 5.51	31	190.0–195.0
Xb	$C_{22}H_{20}N_2O_4$	376.41	70.20 70.32	5.36 5.42	7.44 7.32	0.4	230.0[a]

a) Decomposing.

polar starting aldehyde *IV* (Fig. 3).

Synthesis of 4-(dimethylamino)-2-hydroxybenzaldehyde (*VI*) was performed by the Vilsmeier–Haack formylation. The reaction gave product *VI* in a 66 % yield. A small amount of by-product *VIa* was also obtained (Fig. 4).

Table 3. Spectral data of newly prepared compounds

Compound	Spectral data
VIIa[a]	IR, $\tilde{\nu}$/cm^{-1}: 3300–2366 (br m, COOH), 1722 (s, C═O), 1691 (s, C═O), 1610 (m, C═C), 1455 (m), 1428 (m), 1390 (m), 1343 (m), 1289 (w), 1243 (s, C—O from lactone), 1189 (m), 1116 (w), 1073 (m), 919 (br m), 853 (w), 787 (m), 749 (s), 664 (w) ^{1}H NMR (DMSO-d_6), δ: 12.53 (br s, 1 H, COOH), 7.99 (s, 1 H, H-4), 7.70 (dd, 1 H, $J_{5,6}$ = 7.7 Hz, $J_{5,7}$ = 1.6 Hz, H-5), 7.61 (ddd, 1 H, $J_{7,8}$ = 8.3 Hz, $J_{6,7}$ = 7.0 Hz, $J_{5,7}$ = 1.6 Hz, H-7), 7.42 (dm, 1 H, $J_{7,8}$ = 8.3 Hz, $w_{1/2} \approx$ 2.5 Hz, among others $J_{6,8}$ = 1.2 Hz, H-8), 7.37 (ddd, 1 H, $J_{5,6}$ = 7.7 Hz, $J_{6,7}$ = 7.0 Hz, $J_{6,8}$ = 1.2 Hz, H-6), 3.51 (s, 2 H, CH_2COO) ^{13}C NMR ($CDCl_3$), δ: 169.0 (s, COOH), 161.5 (s, C-2), 153.5 (s, C-9), 142.0 (d, C-4), 131.6 (d, C-7), 127.8 (d, C-5), 124.6 (d, C-6), 121.9 and 119.0 (2 × s, C-3 and C-10), 116.7 (d, C-8), 35.9 (t, CH_2)
VIIb[a]	^{1}H NMR (DMSO-d_6), δ: 8.44 (s, 2 H, H-4), 7.83 (dd, 2 H, $J_{5,6}$ = 7.8 Hz, $J_{5,7}$ = 1.5 Hz, H-5), 7.43 (ddd, 2 H, $J_{5,6}$ = 7.8 Hz, $J_{6,7}$ = 7.3 Hz, $J_{6,8}$ = 1.0 Hz, H-6), 7.69 (ddd, 2 H, $J_{7,8}$ = 8.3 Hz, $J_{6,7}$ = 7.3 Hz, $J_{5,7}$ = 1.5 Hz, H-7), 7.49 (dm, 2 H, $J_{7,8}$ = 8.3 Hz, $w_{1/2} \approx$ 2.5 Hz, among others $J_{6,8}$ = 1.0 Hz, H-8)
VIIc[a]	^{1}H NMR (DMSO-d_6), δ: 9.93 (s, 1 H, HO—), 8.26 (s, 1 H, H-4), 7.85 (d, 1 H, $J_{11,12}$ = 16.9 Hz, H-12 or H-11), 7.76 (dd, 1 H, $J_{5,6}$ = 7.6 Hz, $J_{5,7}$ = 1.7 Hz, H-5), 7.59 (ddd, 1 H, $J_{7,8}$ = 8.2 Hz, $J_{6,7}$ = 7.4 Hz, $J_{5,7}$ = 1.7 Hz, H-7), 7.56 (dd, 1 H, $J_{17,18}$ = 7.9 Hz, $J_{16,18}$ = 1.5 Hz, H-18), 7.42 (dm, 1 H, $J_{7,8}$ = 8.2 Hz, $w_{1/2}$ = 2.0 Hz, among others $J_{6,8}$ = 1.1 Hz, H-8), 7.37 (ddd, 1 H, $J_{5,6}$ = 7.6 Hz, $J_{6,7}$ = 7.4 Hz, $J_{6,8}$ = 1.1 Hz, H-6), 7.21 (d, 1 H, $J_{11,12}$ = 16.9 Hz, H-11 or H-12), 7.15 (ddd, 1 H, $J_{15,16}$ = 8.3 Hz, $J_{16,17}$ = 7.1 Hz, $J_{16,18}$ = 1.5 Hz, H-16), 6.90 (dd, 1 H, $J_{15,16}$ = 8.3 Hz, $J_{15,17}$ = 1.1 Hz, H-15), 6.84 (ddd, 1 H, $J_{17,18}$ = 7.9 Hz, $J_{16,17}$ = 7.1 Hz, $J_{15,17}$ = 1.1 Hz, H-17) ^{13}C NMR (DMSO-d_6), δ: 159.7 (s, C-2), 155.5 (s, *ipso* C-14), 152.2 (s, *ipso* C-9), 137.0 (d, C-4), 131.1 (d, C-7), 129.4 (d, C-16), 128.4 (d, C-12), 128.2 (d, C-5), 126.9 (d, C-18), 124.6, 124.5, and 123.5 (C-6, C-10, and C-17), 121.5 (d, C-11), 119.6 and 119.4 (C-3 and C-13), 115.9 (d, C-15), 115.8 (d, C-8)
VIIIa[a]	IR, $\tilde{\nu}$/cm^{-1}: 3219 (w, OH), 2925 (m), 2865 (w), 1690 (s, C═O), 1613 (s, C═O), 1459 (m), 1578 (m), 1505 (w), 1378 (m), 1312 (m), 1258 (m), 1223 (m), 1154 (m), 1076 (w), 853 (m), 791 (m) ^{1}H NMR (DMSO-d_6), δ: not seen (1 H, COOH), 7.83 (s, 1 H, H-4), 7.49 (d, 1 H, $J_{5,6}$ = 8.5 Hz, H-5), 6.79 (dd, 1 H, $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.3 Hz, H-6), 6.72 (d, 1 H, $J_{6,8}$ = 2.3 Hz, H-8), 3.41 (s, 1 H, CH_2) ^{13}C NMR (DMSO-d_6), δ: 171.7 (s, COOH), 161.1 (s, C(2)═O), 160.8 (s, C-7), 154.8 (s, C-9), 142.1 (d, C-4), 129.3 (d, C-5), 118.3 (s, C-3), 113.3 (d, C-6), 111.5 (s, C-10), 102.0 (d, C-8), 35.7 (t, CH_2)
VIIIb[a]	^{1}H NMR (DMSO-d_6), δ: 8.26 (s, 2H, C-4), 7.60 (d, 2H, $J_{5,6}$ = 8.5 Hz, C-5), 6.83 (dd, 2H, $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.3 Hz, C-6), 6.77 (d, 2H, $J_{6,8}$ = 2.3 Hz, C-8), not seen (2H, —OH)
VIIIc	IR, $\tilde{\nu}$/cm^{-1}: 3288 (br s, OH), 2925 (s), 2856 (m), 1671 (m), 1621 (m), 1459 (m), 1378 (w), 1258 (m), 1076 (br m), 1015 (br m) ^{1}H NMR (DMSO-d_6), δ: 10.80 (s, 2 H, 2 × —OH), 9.79 (s, 1 H, —OH), 8.42 (s, 1 H, H-4), 7.74 (d, 1 H, $J_{5,6}$ = 8.5 Hz, H-5), 7.47 (d, 1 H, $J_{5,6}$ = 8.5 Hz, H-6), 7.43 (s, 1 H, H-8), 6.97 (s, 1 H, $w_{1/2}$ = 4.7 Hz, H-15), 6.90–6.74 (m, 4 H, H-11, H-12, H-17, and H-18) with higher order multiplicity
IXa[a]	IR, $\tilde{\nu}$/cm^{-1}: 3223 (m), 2922 (s), 2852 (s), 1709 (s, C═O), 1613 (s, C═O), 1567 (m), 1509 (m), 1455 (m), 1385 (m), 1354 (w), 1289 (m), 1242 (m), 1188 (m), 1157 (s), 1119 (w), 1069 (w), 1027 (m), 972 (w), 818 (w), 783 (w), 726 (w)
IXb[a]	^{1}H NMR (DMSO-d_6), δ: 8.32 (s, 2 H, H-4), 7.69 (d, 2 H, $J_{5,6}$ = 8.6 Hz, H-5), 7.04 (s, 2 H, H-8), 6.99 (d, 2 H, $J_{5,6}$ = 8.6 Hz, H-6), 3.89 (s, 6 H, —OMe)
IXc	IR, $\tilde{\nu}$/cm^{-1}: 3624–3061 (br m), 2937 (w), 1710 (s, C═O), 1613 (s), 1505 (w), 1444 (br w), 1262 (m), 1208 (w), 1158 (m), 1031 (m), 799 (m) ^{1}H NMR (DMSO-d_6), δ: 9.94 (s, 1 H, —OH), 8.13 (s, 1 H, H-4), 7.68 (d, 1 H, $J_{11,12}$ = 16.6 Hz, H-11), 7.65 (d, 1 H, $J_{5,6}$ = 8.7 Hz, H-5), 7.45 (d, 1 H, $J_{17,18}$ = 9.5 Hz, H-18), 7.03 (d, 1 H, $J_{11,12}$ = 16.6 Hz, H-12), 7.02 (d, 1 H, $J_{6,8}$ = 2.4 Hz, H-8), 6.97 (dd, 1 H, $J_{5,6}$ = 8.7 Hz, $J_{6,8}$ = 2.4 Hz, H-6), 6.46 (d, 1 H, $J_{15,17}$ = 2.4 Hz, H-15), 6.45 (dd, 1 H, $J_{17,18}$ = 9.5 Hz, $J_{15,17}$ = 2.4 Hz, H-17), 3.86 (s, 3 H, MeO—C(7)), 3.73 (s, 3 H, MeO—C(16))
Xa	^{1}H NMR (DMSO-d_6), δ: 12.36 (br s, 1 H, COOH), 7.76 (s, 1 H, H-4), 7.43 (d, 1 H, $J_{5,6}$ = 8.8 Hz, H-5), 6.73 (dd, 1 H, $J_{5,6}$ = 8.8 Hz, $J_{6,8}$ = 2.4 Hz, H-6), 6.57 (d, 1 H, $J_{6,8}$ = 2.4 Hz, H-8), 3.39 (s, 2 H, CH_2), 3.02 (s, 6 H, —N(Me)$_2$) ^{13}C NMR (DMSO-d_6) HMQC also, δ: 171.9 (s, COOH), 161.6 (s, C-2), 155.3 (s, C-9), 152.5 (s, C-7), 142.3 (d, C-4), 128.6 (d, C-5), 115.6 (s, C-3), 109.3 (d, C-6), 108.3 (s, C-10), 97.1 (d, C-8), 39.1 (q, —N(Me)$_2$), 35.7 (t, CH_2)
Xb	^{1}H NMR (DMSO-d_6), δ: 8.21 (s, 2 H, H-4), 7.53 (d, 2 H, $J_{5,6}$ = 8.9 Hz, H-5), 6.77 (dd, 2 H, $J_{5,6}$ = 8.9 Hz, $J_{6,8}$ = 2.4 Hz, H-6), 6.60 (d, 2 H, $J_{6,8}$ = 2.4 Hz, H-8), 3.06 (s, 12 H, 2 × (Me)$_2$N—)

a) Known compounds with listed spectral data not yet described in literature.

Synthesis of 2-(2-oxo-2*H*-chromen-3-yl)acetic acid (*VIIa*) was performed starting from salicylaldehyde (*III*) in DMF under microwave irradiation (9 × 2 min at the power of 250 W) in a 61 % yield (Fig. 2). Microwave irradiation significantly accelerated the reaction compared to 5 h of heating at 185 ℃ (Ito, 1951) or 1.5 h reflux in $(Et)_3N$ (Bochkov et al., 2008). By-products *VIIb* and *VIIc* were obtained in 14 % and 4 % yields, respectively. The time of irradiation was optimised by monitoring the consumption of salicylaldehyde (*III*) using TLC analysis (Table 1).

Synthesis of 2-(7-hydroxy-2-oxo-2*H*-chromen-3-yl)-acetic acid (*VIIIa*) started from 2,4-dihydroxybenzaldehyde (*IV*) according to the above described pro-

cedure for *VIIa* in a 31 % yield. In this reaction, no DMF solvent was used. DMF caused separation problems because products *VIIIa*–*VIIIc* are polar containing at least one phenolic HO— group (Fig. 2, Table 1).

Syntheses of 2-(7-methoxy-2-oxo-2*H*-chromen-3-yl)acetic acid (*IXa*) and *Xa* were performed similarly to the above procedure described for *VIIa* without the DMF solvent. Reactions were carried out using 2-hydroxy-4-methoxybenzaldehyde (*V*) or 4-(dimethylamino)-2-hydroxybenzaldehyde (*VI*), respectively. All the products *IXa*–*IXc*, *Xa*–*Xb* were isolated and their structures determined (Fig. 2, Table 3). Product *IXa* was prepared also under thermal conditions (4 h at 190 ℃) in a 22 % yield (Hurenkamp et al., 2007).

The last condensation did not result in complete conversion of the starting aldehyde *VI* which is much less reactive compared to *III*–*V*. Conversion of *VI* did not improve even using different reaction conditions (e.g., stronger power of MW, longer reaction time, activation of aldehyde with a catalytic amount of piperidine or eight fold excess of succinic acid anhydride). Within significant prolongation of the microwave irradiation, the polymerisation took place. The last reaction was exceptional also due to low abundance of by-product *Xb* (0.4 %) and no occurrence of *Xc*.

Composition and properties of the corresponding new products are summarised in Tables 2 and 3.

All 2-(2-oxo-2*H*-chromen-3-yl)acetic acids (*VIIa*–*Xa*) possessed intensive yellow fluorescence at the mass concentration of 2 mg mL^{-1} of DMSO under UV light at 254 nm. The intensity of fluorescence was not quantified. It was evident that the power of fluorescence depends on the present substituent in the increasing order: H—, MeO—, HO—, Me_2N—. Thus prepared compounds could also be used as fluorescent markers in molecular biology as well as in material chemistry.

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