

New 1-hetarylfuopyridines and chromenes based on pyridoxal and 4-hydroxycoumarin

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Experimental section

Spectroscopic measurements

NMR experiments were performed on a Bruker AVANCE-400 spectrometer at 303 K equipped with 5 mm broadband probehead working at 400.13 MHz in ^1H and 100.61 MHz in ^{13}C experiments. Chemical shifts in ^1H spectra were reported relative to the solvent as internal standard (DMSO- d_6). MALDI mass spectra were obtained on an ULTRAFLEX III mass spectrometer. Measurements were conducted with the use of plastic and metal plates. 2,5-Dihydroxybenzoic acid (2,5-DHB) was used as matrix. IR spectra were recorded on a Tensor-27 spectrometer of Bruker Company in the range of 400-3600 cm^{-1} in KBr pellets.

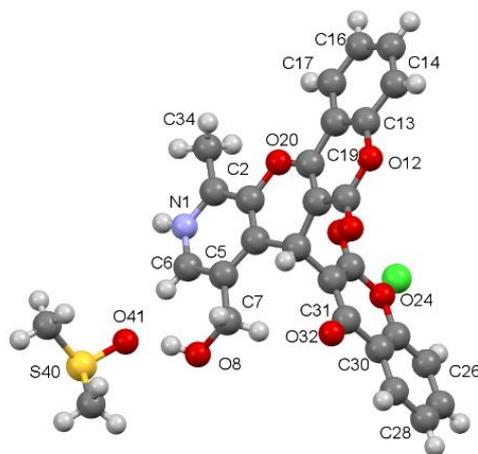
The X-ray diffraction data for the compounds 5.

$2(\text{C}_{26}\text{H}_{17}\text{N}\text{O}_7) \times 2(\text{C}_2\text{H}_6\text{O}_5) \times \text{Cl}$ ($M=1102.52$), monoclinic, space group $C2/c$ at 294 K: $a = 25.553(4)$, $b = 13.0547(19)$, $c = 16.853(2)$ Å, $\beta = 101.570(7)^\circ$, $V = 5507.7(14)$ Å 3 , $Z = 4$, $d_{\text{calc}} = 1.330$ g cm^{-3} ; $\mu(\text{Mo-K}\alpha) = 0.216$ mm^{-1} ; $F(000) = 2292$. Total of 36001 reflections were collected (5409 independent reflections with $\theta < 26^\circ$, $R_{\text{int}} = 0.110$) and used in the refinement, which converged to wR_2 0.3743, GOOF 1.21 for all independent reflections [$R_1 = 0.1048$ was calculated for 2780 reflections with $I \geq 2\sigma(I)$].

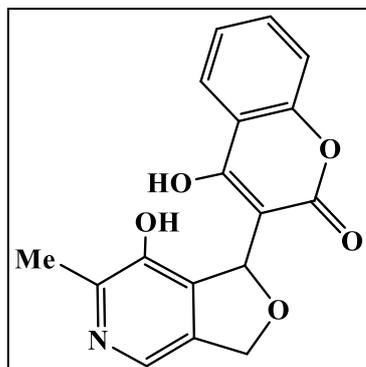
X-ray diffraction analysis was performed at room temperature on automatic diffractometer Bruker Kappa Apex II CCD diffractometer using graphite monochromated $\text{MoK}\alpha$ (0.71073 Å) radiation and ω -scan rotation. Data collection: images were indexed, integrated, and scaled using the APEX2^{S1} data reduction package and corrected for absorption using SADABS.^{S2} The structure

of compound **6** was solved by the direct methods and refined using SHELX.^{S3} Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were calculated on idealized positions and refined as riding atoms. All calculations were performed using WinGX.^{S4} Intermolecular interactions were analyzed using the program PLATON.^{S5} All the figures were produced by the MERCURY program.^{S6} Bad experimental data from crystal of compound **6** are due to a weakly reflecting crystal.

CCDC 2018191 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* <http://www.ccdc.cam.ac.uk>.

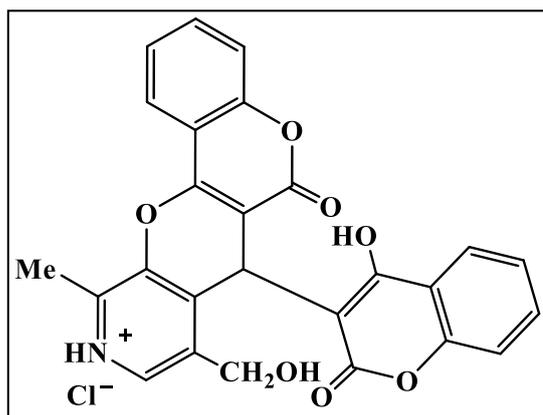


Synthesis



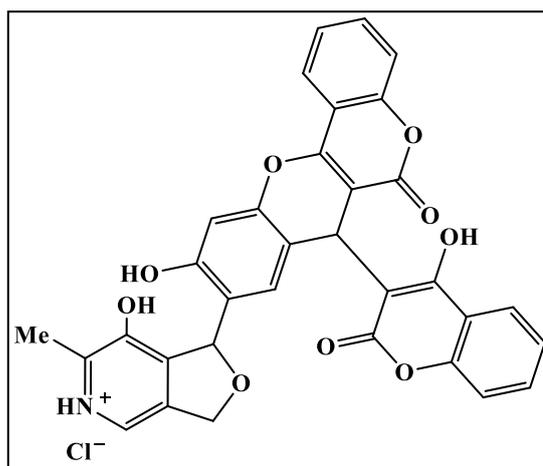
4-Hydroxy-3-(7-hydroxy-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-1-yl)-2H-chromen-2-one (**4**)

A mixture of pyridoxal **1** (0.5 g, 2.99 mmol), absolute ethanol (10 ml) and 4-hydroxycoumarin **2** (0.48 g, 2.99 mmol) was refluxed for 10 h. The precipitate was filtered, washed with alcohol and diethyl ether, and dried under vacuum. Yield of **4** was 0.90 g (97%). M.p. > 300 °C. IR spectrum, ν , cm^{-1} : 456, 597, 758, 935, 1047, 1086, 1218, 1256, 1351, 1397, 1511, 1561, 1601, 1626, 2067, 2607, 3422. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$), δ : 2.44 s (3H, CH_3), 5.13 d (1H, CH_2 , J 12.4 Hz), 5.60 dd (1H, CH_2 , J 12.3, 2.7 Hz), 6.64 d (1H, CH, J 2.6 Hz), 7.17 d (1H, $\text{CH}_{\text{coum.}}$, J 8.1 Hz), 7.21 t (1H, $\text{CH}_{\text{coum.}}$, J 7.5 Hz), 7.47 td (1H, $\text{CH}_{\text{coum.}}$, J 7.7, 1.7 Hz), 7.88 dd (1H, $\text{CH}_{\text{coum.}}$, J 7.8, 1.8 Hz), 8.14 s (1H, $\text{CH}_{\text{arom.}}$). ^{13}C NMR($\text{DMSO}-d_6$), δ : 15.04, 72.14, 78.72, 100.00, 116.14, 121.36, 123.10, 124.51, 124.72, 131.45, 137.71, 141.07, 143.78, 149.82, 153.93, 161.09, 171.81. MS (MALDI), m/z : 312.2 $[\text{M}+\text{H}]^+$. Found, %: C 65.47; H 4.11; N 4.52. $\text{C}_{17}\text{H}_{13}\text{NO}_5$. Calculated, %: C 65.59; H 4.21; N 4.50.



7-(4-Hydroxy-2-oxo-2H-chromen-3-yl)-8-hydroxymethyl-11-methyl-6-oxo-6H,7H-chromeno[3',4':5,6]pyrano[2,3-c]pyridin-10-ium chloride (5)

A mixture of pyridoxal hydrochloride **1**·HCl (0.5 g, 2.45 mmol), absolute ethanol (10 ml), and 4-hydroxycoumarin **2** (0.79 g, 4.90 mmol) was refluxed for 10 h. The precipitate was filtered, washed with alcohol and diethyl ether, and dried under vacuum. Yield of **5** 0.40 g (67%). M.p. = 248 °C (dec.). IR spectrum, ν , cm^{-1} : 414, 458, 513, 559, 664, 693, 739, 746, 758, 782, 894, 924, 1058, 1093, 1108, 1200, 1218, 1278, 1351, 1374, 1385, 1406, 1465, 1529, 1590, 1601, 1613, 1642, 1712, 2555, 3090, 3445. ^1H NMR spectrum (400 MHz, DMSO- d_6), δ : 2.68 s (3H, CH₃), 4.39 d (1H, CH₂, J 14.5 Hz), 4.68 d (1H, CH₂, J 14.5 Hz), 5.63 s (1H, CH), 7.28 d (1H, CH_{coum.}, J 8.2 Hz), 7.33 br.t (1H, CH_{coum.}, J 7.7 Hz), 7.41 d (1H, CH_{coum.}, J 8.3 Hz), 7.48 t (1H, CH_{coum.}, J 7.7 Hz), 7.58 ddd (1H, CH_{coum.}, J 8.5, 7.2, 1.6 Hz), 7.68 ddd (1H, CH_{coum.}, J 8.6, 7.4, 1.6 Hz), 8.03 br. d (1H, CH_{coum.}, J 8.0 Hz), 8.07 dd (1H, CH_{coum.}, J 7.9, 1.6 Hz), 8.30 s (1H, CH_{arom.}). ^{13}C NMR(DMSO- d_6), δ : 18.90, 26.89, 57.92, 100.69, 104.36, 114.06, 116.67, 116.91, 116.94, 123.03, 124.24, 124.50, 125.14, 127.92, 132.69, 133.10, 134.65, 142.82, 144.34, 145.25, 152.35, 152.94, 156.28, 160.53, 161.58, 162.86. MS (MALDI), m/z : 456.4 [M-Cl]⁺. Found, %: C 61.72; H 3.60; Cl 7.63; N 2.29. C₂₆H₁₈ClNO₇. Calculated, %: C 63.49; H 3.69; Cl 7.21; N 2.85.



7-Hydroxy-1-[10-hydroxy-7-(4-hydroxy-2-oxo-2H-chromen-3-yl)-6-oxo-6H,7H-chromeno[4,3-b]chromen-9-yl]-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride (7)

To a suspension of aldehyde **6** (0.5 g, 1.54 mmol) and TsOH (0.1 g) in absolute ethanol (10 ml), 4-hydroxycoumarin **2** (0.5 g, 3.09 mmol) was added in portions on stirring. The mixture was refluxed for 3 h. The precipitate was filtered, washed with diethyl ether, and dried under vacuum. Yield of **7** 0.94 g (98%). M.p. = 250°C (dec.). IR spectrum, ν , cm^{-1} : 567; 683; 759; 1034; 1116; 1202; 1389; 1492; 1560; 1609; 1646; 1681; 1704; 2360; 2924; 3077; 3271; 3410. ^1H NMR spectrum (400 MHz, DMSO- d_6), δ : 2.43 s (3H, CH₃), 5.07 d (1H, CH₂, J 12.8 Hz), 5.15 dd (1H, CH₂, J 12.8, 2.2 Hz), 5.53 br. s (1H, CH), 6.40 br. d

(1H, CH, J 2.4 Hz), 6.77 s (1H, Rz), 6.93 s (1H, Rz), 7.33 d (1H, CH_{coum.}, J 8.4 Hz), 7.38 d (1H, CH_{coum.}, J 6.9 Hz), 7.43-7.51 m (3H, CH_{coum.}), 7.61 ddd (1H, CH_{coum.}, J 8.6, 7.3, 1.5 Hz), 7.70 ddd (1H, CH_{coum.}, J 8.6, 7.4, 1.6 Hz), 8.06 s (1H, CH_{arom.}), 8.09 dd (1H, CH_{coum.}, J 8.0, 1.6 Hz). ¹³C NMR(DMSO-*d*₆), δ : 16.76, 28.70, 71.43, 79.93, 104.15, 114.32, 116.67, 116.88, 116.94, 123.15, 124.36, 124.98, 126.02, 128.65, 132.50, 132.86, 137.32, 143.63, 145.77, 149.50, 150.02, 152.41, 152.69, 155.53, 156.72, 160.95. MS (MALDI), m/z : 576.1[M-Cl]⁺. Found, %: C 64.72; H 3.60; Cl 5.63; N 2.39. C₃₃H₂₂ClNO₉. Calculated, %: C 64.77; H 3.62; Cl 5.79; N 2.29.

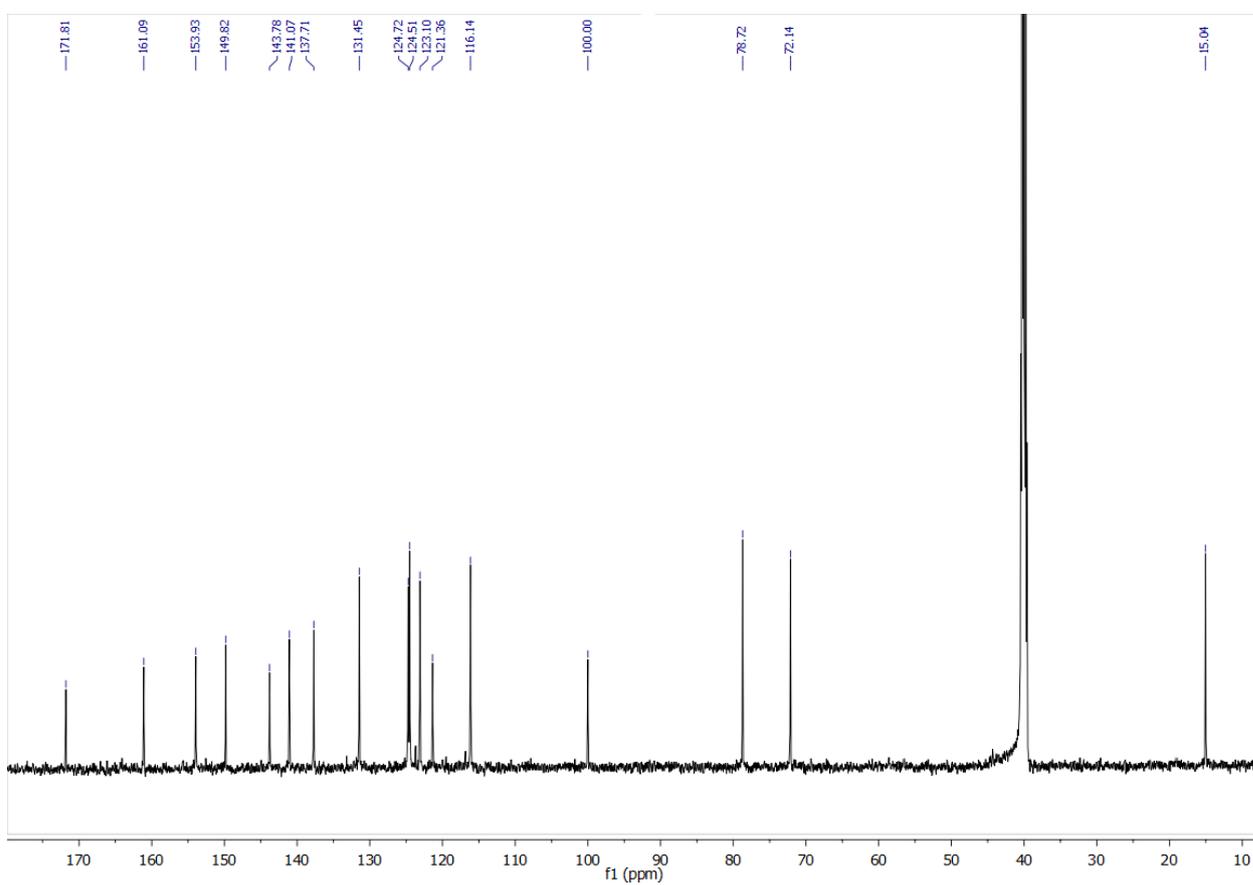
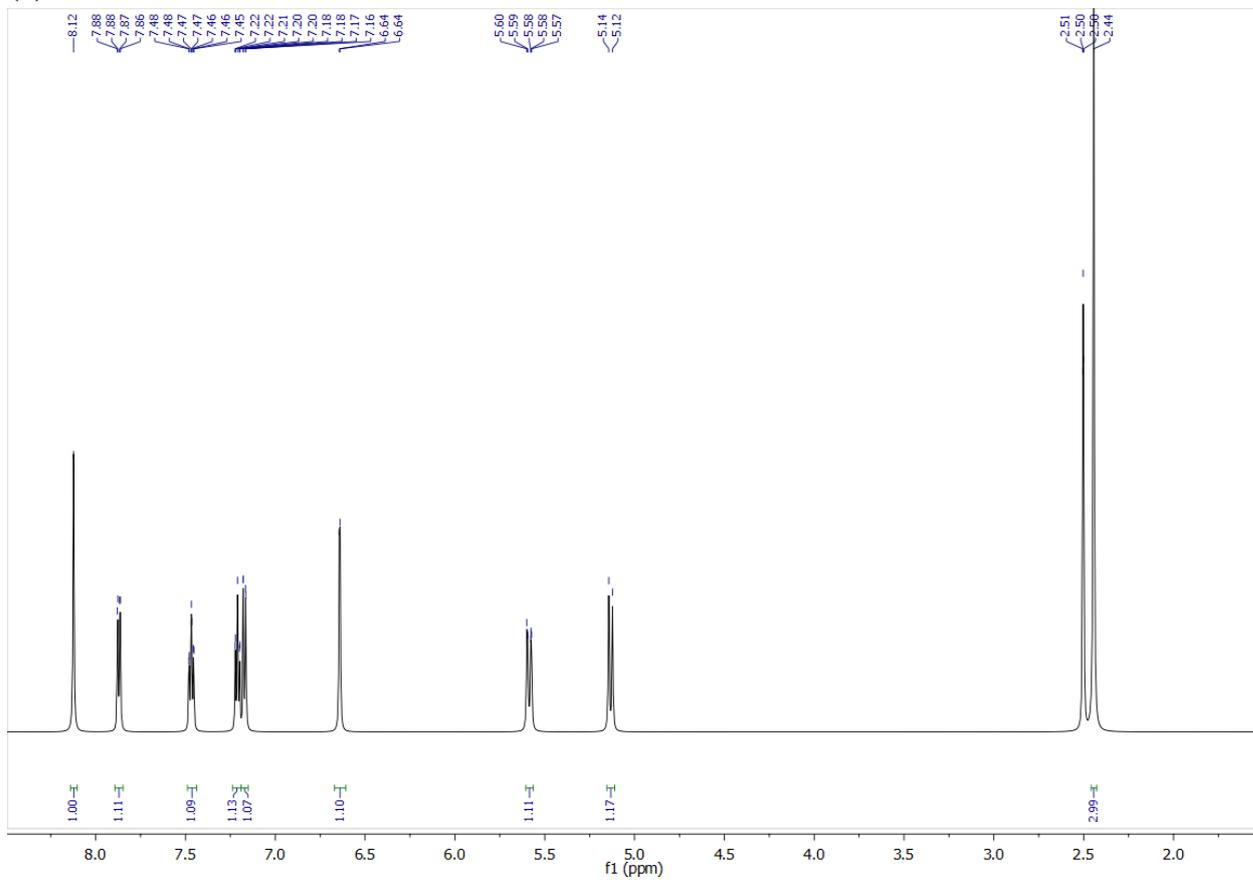
The authors are grateful to the Collective Spectral-Analytical Center of Physicochemical studies of structure, properties, and composition of substances and materials of the Federal Research Center of the Kazan Scientific Center of RAS for technical support of the studies. X-ray studies were performed using the equipment of the Federal Research Center Kazan Scientific Center of RAS.

References

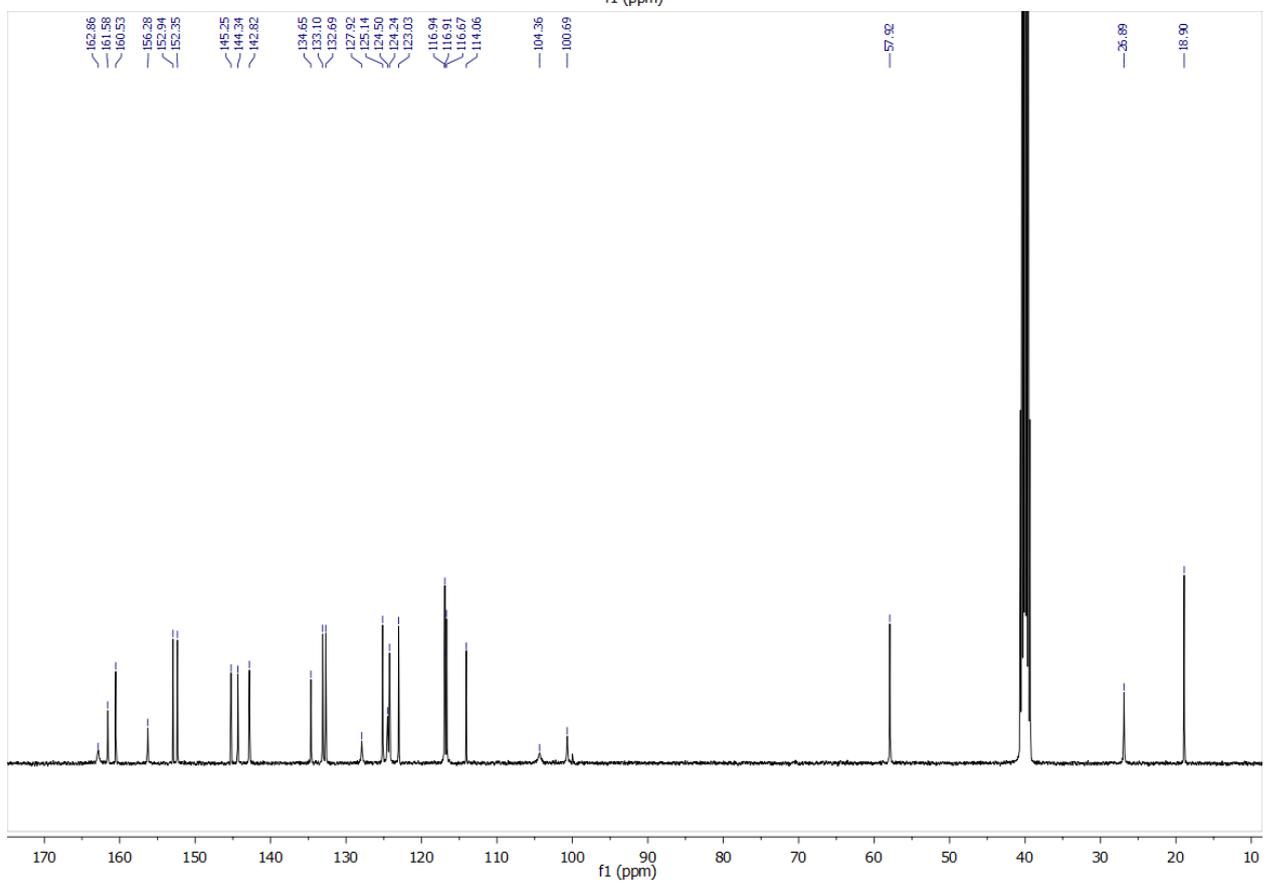
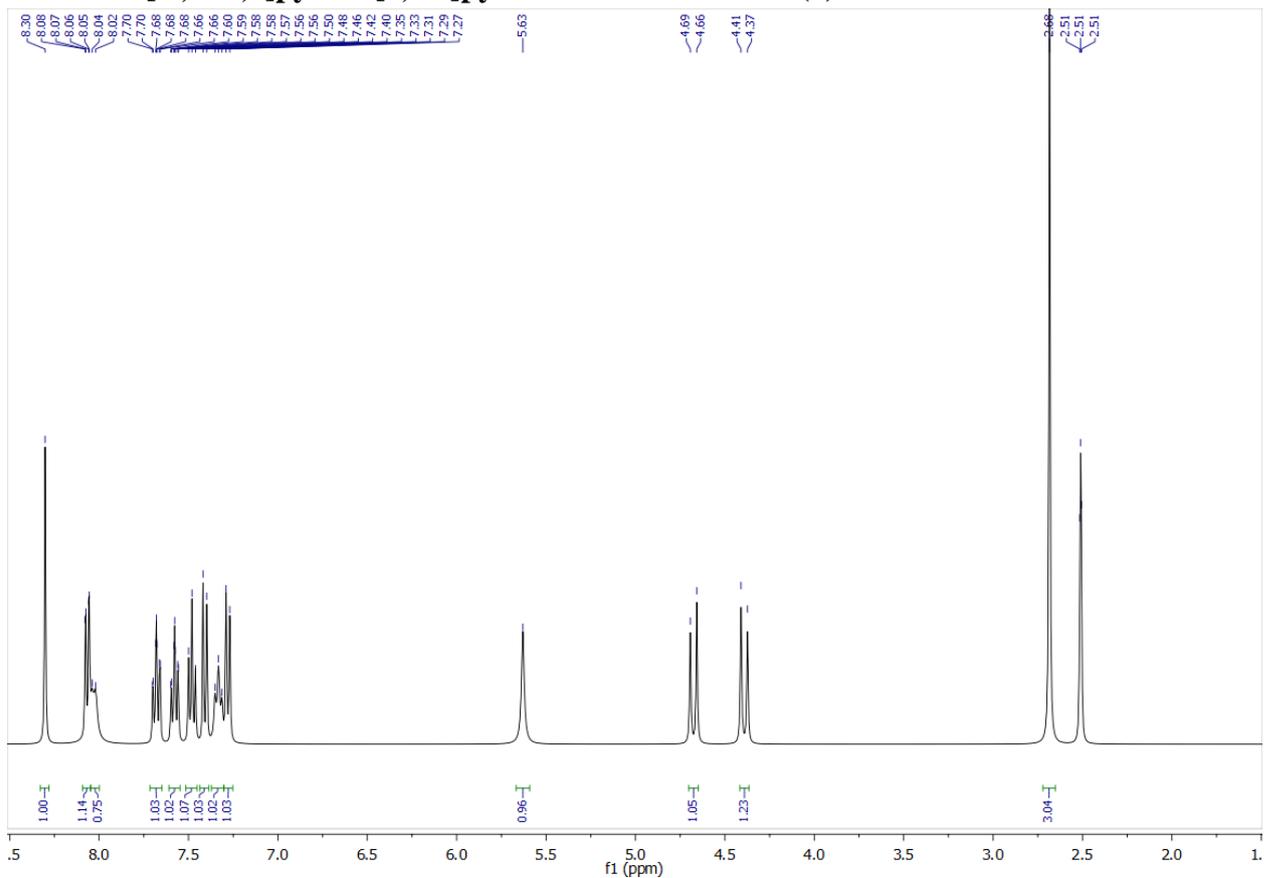
- S1. APEX2 Version (2.1), SAINTPlus. Data Reduction and Correction Program Version 7.31A, Bruker Advanced X-ray Solutions, Bruker AXS Inc., Madison, Wisconsin, USA, 2006.
- S2. G.M. Sheldrick. SADABS, Program for empirical X-ray absorption correction, Bruker-Nonius, 1990-2004.
- S3. G. M. Sheldrick, SHELX programs, *Acta Crystallogr.*, 2015, **C71**, 3.
- S4. L. J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837.
- S5. A. L. Spek, *Acta Crystallogr.*, 2009, **D65**, 148.
- S6. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek and P. A. Wood, *J. Appl. Crystallogr.*, 2008, **41**, 466.

Copies of NMR spectra for the compounds

4-Hydroxy-3-(7-hydroxy-6-methyl-1,3-dihydrofuro[3,4-*c*]pyridin-1-yl)-2*H*-chromen-2-one (4)



7-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-8-hydroxymethyl-11-methyl-6-oxo-6*H*,7*H*-chromeno[3',4':5,6]pyrano[2,3-*c*]pyridin-10-ium chloride (5)



7-Hydroxy-1-[10-hydroxy-7-(4-hydroxy-2-oxo-2H-chromen-3-yl)-6-oxo-6H,7H-chromeno[4,3-b]chromen-9-yl]-6-methyl-1,3-dihydrofuro[3,4-c]pyridin-5-ium chloride (7)

