

Ferrocene-Containing Gallic Acid-Derivative Modified Carbon-Nanotube Electrodes for the Fast Simultaneous and Selective Determination of Cytostatics from Aqueous Solutions

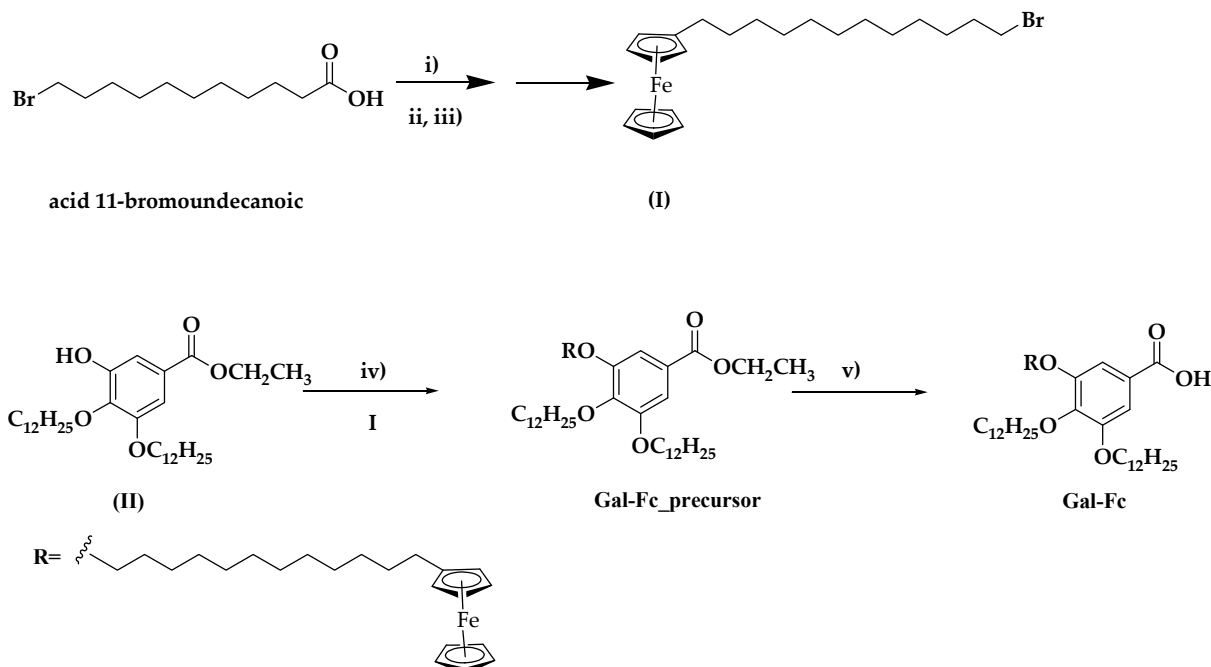
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1. Experimental section



Scheme S1. Synthetic pathway for the synthesis of Gal-Fc. Reagents and conditions: (i) SOCl_2 , toluene, 70°C , inert atmosphere, 24 h; (ii) ferrocene, AlCl_3 , DCM, 0°C , inert atmosphere, 24 h at r.t.; (iii) AlCl_3 , NaBH_4 , THF, 0°C , inert atmosphere, 24 h at r.t.; (iv) K_2CO_3 , DMF, 80°C , 24 h; (v) KOH , EtOH, ΔT .

Compound I was obtained according to a previously published procedure.[1]

Synthesis of compound II:

Ethyl 3,4,5-trihydroxybenzoate (1.0 g, 5.05 mmol) and K_2CO_3 (1.34 g, 10.1 mmol) in 20 mL cyclohexanone were mechanically stirred at 60°C for 30 minutes, and then, 1-bromododecane (2.52 g, 10.1 mmol) was quickly added. The reaction mixture was stirred at 90°C overnight, then cooled to room temperature, filtered over celite, and the solvent was evaporated. The residue was taken in DCM, washed with water (3 × 150 mL) and brine (1 × 100 mL), then the organic phase was dried over anhydrous Na_2SO_4 , filtered, and taken to dryness. The pure product was obtained using column chromatography (SiO_2 /chloroform:hexane = 1:1) as a white solid (2.4 mmol, 47%).

1H NMR (300 MHz, Chloroform- d , δ /ppm): 7.32 (d, J = 1.8 Hz, 1H), 7.18 (d, J = 1.9 Hz, 1H), 5.87 (s broad, 1H, -OH), 4.15 (t, J = 6.7 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 4.09 (m, 2H), 1.79 (overlapped peaks, 4H), 1.56 – 1.18 (overlapped peaks, 38 H), 0.89 (t, 3 J = 6.6 Hz, 6H).

Synthesis of Gal-Fc: Compound II (1.00 g, 1.87 mmol) and K_2CO_3 (0.80 g, 5.75 mmol) in DMF was stirred at 60°C for 30 minutes, followed by the addition of compound I in DMF. The temperature was set at 80°C, and it was stirred at this temperature overnight. After the evaporation of the solvent, the residue was taken with DCM and washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4 , filtered, and dried under reduced pressure. The pure product was isolated after purification on column chromatography on SiO_2 , using hexane:AcOEt = 9:1 as eluent, as a yellow glassy solid.

1H NMR (300 MHz, Chloroform- d) δ 7.27 (d, J = 1.6 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 4.13 – 3.98 (m, 16H), 2.42 – 2.19 (m, 2H), 1.79 (ddd, J = 22.0, 8.5, 6.4 Hz, 6H), 1.57 – 1.35 (m, 12H), 1.29 (d, J = 5.9 Hz, 48H), 0.90 (t, J = 6.5 Hz, 6H).

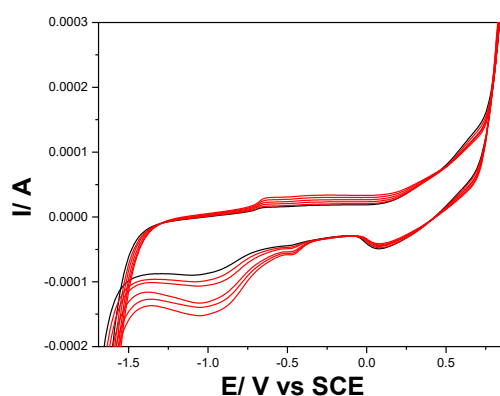
FT-IR (KBr, cm^{-1}): $\nu_{C-H, Fc}$ (3097), $\nu_{CH_2, as}$ (2925), $\nu_{CH_2, s}$ (2854), $\nu_{C=O}$ (1719), $\nu_{Cp-Fe, Fc}$ (485).

The above isolated compound was hydrolyzed in a basic media (using 2 eq KOH) in ethanol/thf mixture under reflux. After the completion of the reaction, the mixture was concentrated under reduced pressure and water was added, acidified with HCl to neutral pH, and the formed precipitate was isolated through filtration. Further, the pure compound was obtained after purification on SiO_2 , using hexane:AcOEt = 9:1 to hexane:AcOEt = 7:3 as eluent.

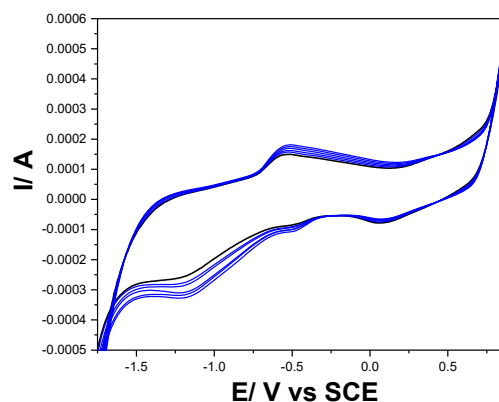
1H NMR (300 MHz, Chloroform- d) δ 7.32 (s, 2H), 4.14 – 3.99 (overlapped, 15H), 2.44 – 2.20 (m, 2H), 1.91 – 1.69 (m, 6H), 1.57 – 1.26 (m, 55H), 0.90 (t, J = 6.5 Hz, 6H).

FT-IR (KBr, cm^{-1}): $\nu_{C-H, Fc}$ (3098), $\nu_{CH_2, as}$ (2925), $\nu_{CH_2, s}$ (2855), $\nu_{C=O}$ (1678), $\nu_{Cp-Fe, Fc}$ (485).

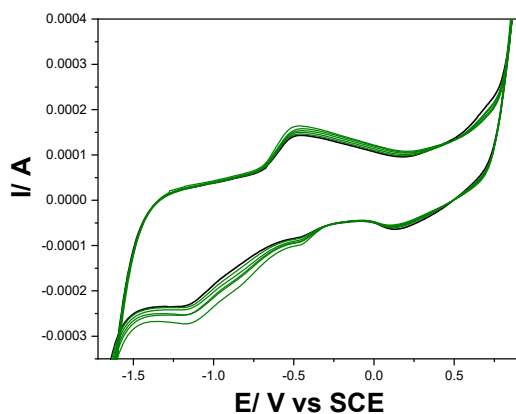
Elemental analysis: Anal. Calcd. for $C_{52}H_{84}FeO_5$ (845.07 $g \cdot mol^{-1}$): C, 73.91; H, 10.02. Found: C, 73.73; H, 9.98.



(a)



(b)



(c)

Figure S1. CVs recorded with Gal-Fc-CNT electrode in 0.1 M NaOH supporting electrolyte within the potential range from -2.00 to +1.00 V/SCE at the scan rate of 0.05 V·s⁻¹ in the presence of (a) 1-5 mg·L⁻¹CPP (red line); (b) 1-5 mg·L⁻¹CPB (blue line); (c) 1-5 mg·L⁻¹DOX (green line).

Table S1. The electroanalytical performance obtained with Gal-Fc-CNT paste electrode.

Technique/ Conditions	Analyte	Peak potential V vs. SCE	Sensitivity ($\mu\text{A} \cdot \text{mg} \cdot \text{L}^{-1}$)	LOD ($\text{mg} \cdot \text{L}^{-1}$)	LQ ($\text{mg} \cdot \text{L}^{-1}$)	RSD (%)	Correlation coefficient (R^2)
DPV/pH=3	DOX	-0.46	40.25	0.0068	0.022	1.38	0.930
		+0.45	269.5	0.0028	0.0093	0.49	0.917
SWV/pH=3	DOX	+0.47	1430	0.00075	0.0025	0.50	0.981
DPV/pH=12	DOX	-0.20	73.71	0.00071	0.0024	0.11	0.992
	CPB	-0.20	5.00	0.055	0.183	1.45	0.840
	CPP	-0.20	6.55	0.044	0.146	1.55	0.829
SWV/pH=12	DOX	-0.60	311.9	0.0078	0.026	3.46	0.990
	CPB	-0.60	22.90	0.013	0.044	0.14	0.849
	CPP	-0.60	30.25	0.009	0.030	0.13	0.827

Table S2. Recovery degrees achieved with Gal-Fc-CNT paste electrode using SWV for tap water spiked with known cytostatic concentrations.

pH	Compound	Spiked concentration ($\mu\text{g}\cdot\text{L}^{-1}$)	Measured concentration ($\mu\text{g}\cdot\text{L}^{-1}$)	Recovery (%)
12	DOX	50	51.25	102.50
			51.80	103.60
			52.125	104.25
	CPB	100	98.75	98.75
			99.20	99.20
			99.80	99.80
	CPP	100	97.40	97.40
			98.10	98.10
			98.50	98.50
3	DOX	50	50.60	101.20
			51.70	103.40
			52.40	104.80
	CPB	100	-*	-
	CPP	100	-	-

*no signal

References

[1] Popa, E.; Andelescu, A.A.; Ilies (b. Motoc), S.; Visan, A.; Cretu, C.; Scarpelli, F.; Crispini, A.; Manea, F.; Szerb, E.I. Hetero-Bimetallic Ferrocene-Containing Zinc(II)-Terpyridyl-Based Metallomesogen: Structural and Electrochemical Characterization. *Mater.* **2023**, *16*(5), 1946. doi: 10.3390/ma16051946