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New series of *γ*-pyrone based podands: synthesis, characterization and study of their application in acetate salts cation trapping for nucleophilic substitution reactions

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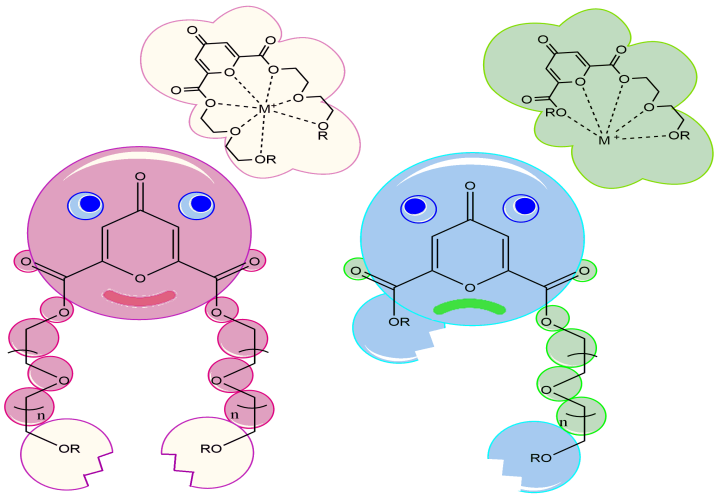
Abstract

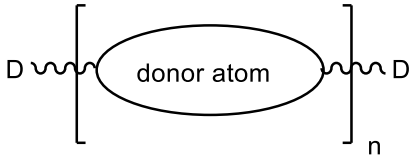
Dialkyl 4-oxo-4*H*-pyran-2,6-dicarboxylates are synthesized *via* esterification of chelidonic acid or *via* intramolecular cyclization of dialkyl-2,4,6-trioxoheptanedioates. Reaction of the dialkyl 4-oxo-4*H*-pyran-2,6-dicarboxylates with a variety of glycol monoalkyl ethers produces a series of new podands in good yields. To demonstrate the use of these podands in cation trapping, nucleophilic substitution reactions are carried out with various acetate salts. The results indicate that the cation diameter's compatibility with binding site leads to the best yield of reaction.



Keywords: Podand, 4*H*-pyran, cation trap, chelidonic acid, esterification reaction

Introduction

The term podand was first introduced by Vögtle and Weber in 1979,[1] and it is derived from the combination of the words "pod" and ligand.[2] The general structure of podands is illustrated in Figure 1.



Podand

Figure 1. General podand structure.

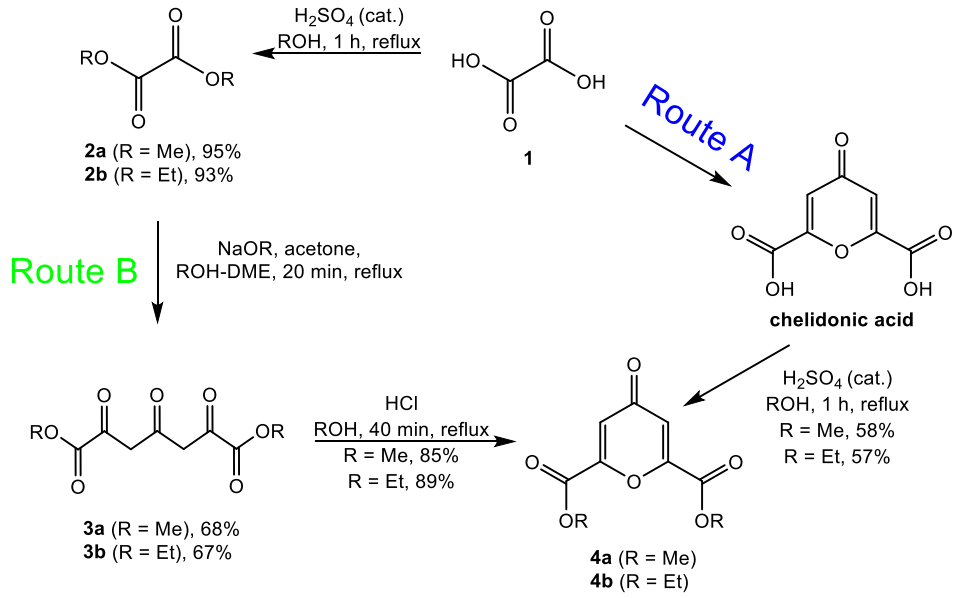
One important behavior of multidentate acyclic ligands (podand), is the ability to form complexes with cations and metals, *i.e.*, they can behave as crown ethers.[3,4] Podands can be used in anion sensors with effect on the fluorescence emission.[5] Podand-type receptors offer advantages compared to rigidly preorganized macrocyclic systems because their binding and release are generally fast.[6-9]

4*H*-Pyran-based podands are one of the most notable classes of podands and several types have been reported.[10] 4*H*-Pyrans are important six-membered heterocycles,[11-13] that have attracted much attention because of their potential utility in applications such as: photochromic materials,[14] organic light-emitting diodes (OLEDs),[15,16] solar cells,[17] and pharmaceutical chemistries etc.[18,19]

Herein, as with previous studies on 4*H*-pyran-4-ones,[20-23] we synthesize some new 2,6-disubstituted 4*H*-pyran-4-one podands. FT-IR, ^{1}H and ^{13}C NMR, mass spectrometry and elemental analysis were used to confirm the structure of the synthesized compounds.

Results and Discussion

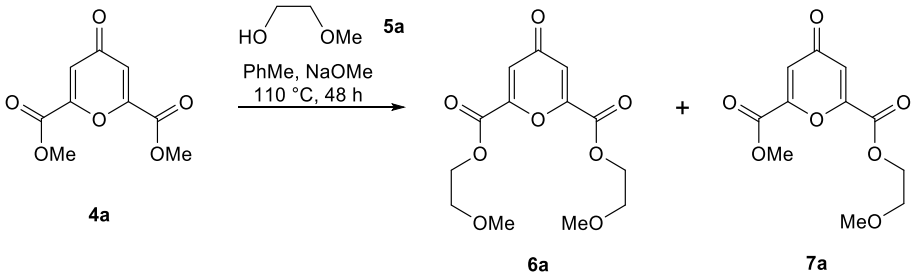
4-Oxo-4*H*-pyran-2,6-dicarboxylic acid (chelidonic acid) was used for the synthesis of dialkyl 4-oxo-4*H*-pyran-2,6-carboxylates according to a literature prcedure.[24] In this method, esterification of chelidonic acid with the appropriate alcohol was performed in the presence of an inorganic or Lewis acid. In a modified procedure,[25] to improve the yield of product, we prepared *via* esterification the methyl and ethyl dialkyl oxalates from oxalic acid with methanol and ethanol, respectively. Condensation of obtained dialkyl oxalates with acetone in the presence of alcoholic solution of related base gave dialkyl-2,4,6-trioxoheptanedioate. Intramolecular cyclization of these compounds in acidic condition afforded the desired products (Scheme 1).



Scheme 1. Synthesis of dialkyl 4-oxo-4*H*-pyran-2,6-carboxylates **4** *via* the traditional method (Route A);[24] and *via* the modified procedure (Route B).[25]

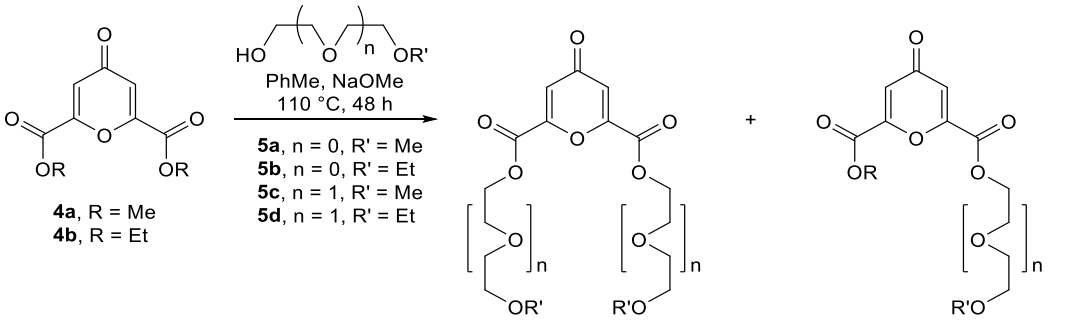
Subsequently, the dialkyl 4-oxo-4*H*-pyran-2,6-dicarboxylates **4a** and **4b** were reacted with a variety of glycol monoalkyl ethers in dry toluene in the presence of catalytic amount of sodium methoxide. Since the use of a 1:1 stoichiometry of reactants led to unreacted starting materials or only trace amount of the desired product (Table 1, entry 1), we optimized the reaction conditions by screening different ratios of **4a:5a** (Table 1).

Table 1. Optimization of the reaction of 4-oxo-4*H*-pyran-2,6-dicarboxylate **4a** with ethylene glycol monomethyl ether **5a** at 110 °C for 48 h.



Entry	4a:5a	Yield of 6a (%)	Yield of 7a (%)
1	1:1	-	10
2	1:1.5	3	9
3	1:2	8	11
4	1:2.5	23	9
5	1:3	40	15
6	1:3.5	64	16
7	1:4	65	16

Finally, by applying a 1:3.5 stoichiometric ratio between dialkyl 4-oxo-4*H*-pyran-2,6-carboxylate to glycol, we produced bis-substituted products with acceptable yield (Scheme 2). Nevertheless, under these reaction conditions minor quantities of the mono-substituted podands were still present in the reaction mixture. The molecular structures of the products were supported by ^{1}H, ^{13}C NMR, mass and FT-IR spectra and elemental analysis. Figure 2 shows the ^{1}H NMR spectra of compounds **6c** and **7c** as representatives of the synthesized bis- and mono-substituted podands, respectively. In the ^{1}H NMR spectrum of the bis-substituted compound **6c** the peak integrals for the etheric protons are in the range of 3.38-3.82 ppm and are doubled compared to the mono-substituted podand **7c**. Absence of the singlet peak at 4.00 ppm related to the unsubstituted methyl carboxylate group, supports further the formation of the bis-substituted derivative **6c**.



Scheme 2. Reaction of dialkyl chelidonates **4** with appropriate glycol monoalkyl ethers

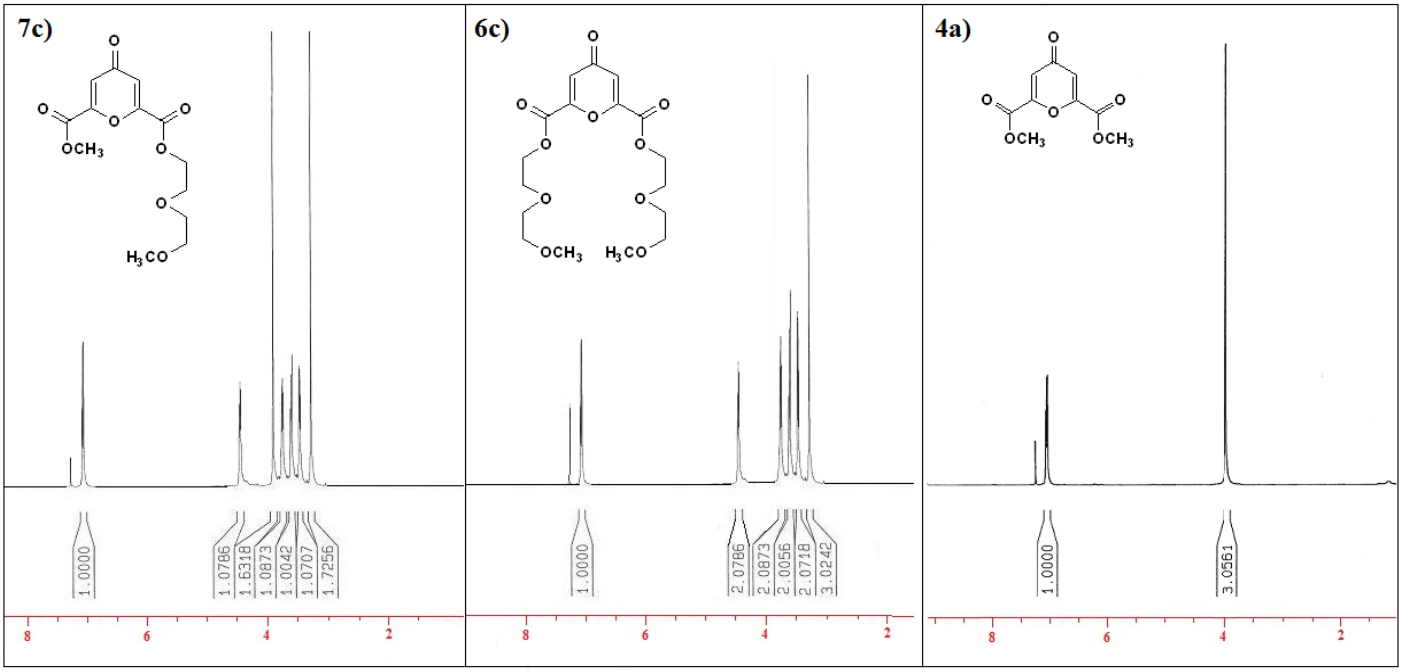


Figure 2. ^{1}H NMR spectra of the **6c** and **7c** as representative of synthesized podands.

The podands ability to trap cations was then examined. For this purpose, 4-chlorobutylferrocene (**8a**)[26] and 4-bromobutylferrocene (**8b**)[27] were synthesized and attempts were made to convert them into 4-ferrocenylbutyl acetate *via* nucleophilic substitution using acetate salts. Initially, as a control experiment we tested the reaction in the absence of podands. 4-Chloro- and 4-bromobutylferrocenes **8a** and **8b**, respectively, were treated with sodium acetate (1 equiv) in MeCN heated at reflux but after 72 h, no product formation was observed (by TLC). Using the same conditions, but in the presence of catalytic amounts of podands the 4-ferrocenylbutyl acetate **9** was formed in good yields (49-74%) after 24 h.

Comparison between the ^{1}H NMR spectra of 4-halobutylferrocene and 4-ferrocenylbutyl acetate is illustrated in Figure 3. The shift of CH_2 peaks (related to protons adjacent to halogen) at 3.55 (CH_2-Cl) or 3.42 (CH_2-Br) ppm to 4.06 ppm (covered with Cp protons, ascribed to protons adjacent to oxygen) and appearance of acetyl CH_3 protons at 2.04 ppm as a singlet peak were clear indications of intended product formation.

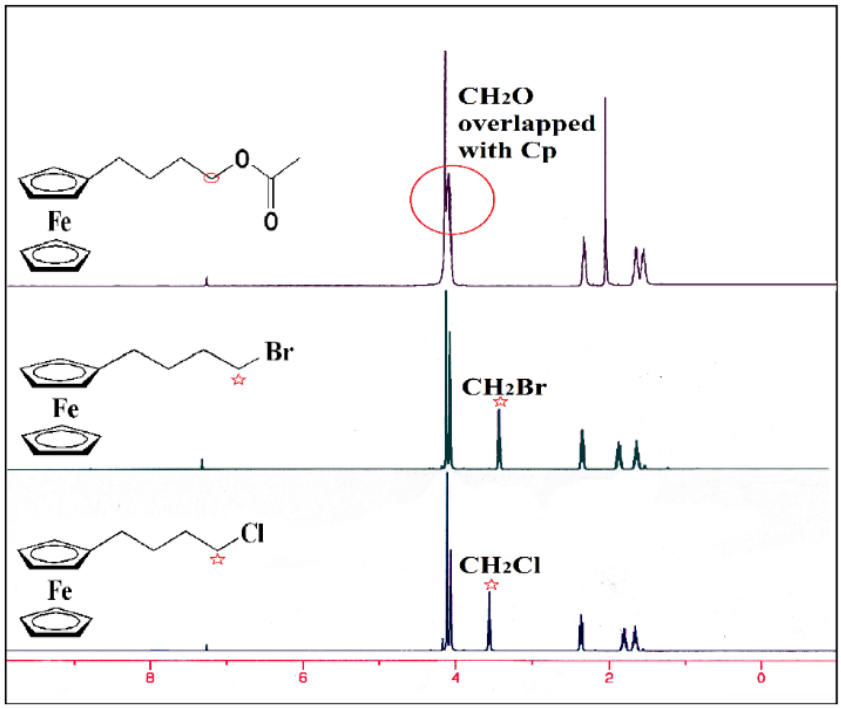
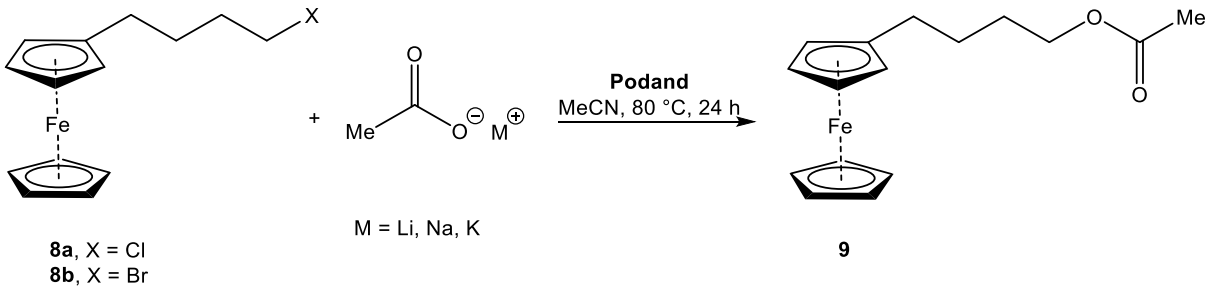


Figure 3. ^{1}H NMR spectra of 4-halobutylferrocenes **8a** and **8b** and 4-ferrocenylbutyl acetate **9**.

Two factors affect the product yields: (1) the leaving group ability of the halide; and, (2) the size of acetate counterion (*i.e.*, the cation). Best result was observed for bromine in Table 2 due to the high leaving ability of bromide in compared with chloride. The synthesized podands are soluble in a variety of organic solvents and can complex with the cations. In the other words, cations can coordinate with oxygen atoms of the podand. The cation diameter plays an important role here; since $K^+ > Na^+ > Li^+$; the best yield was obtained when the lithium salt was used. This result is due to small radius of Li^+ that led to its tighter coordination by the podand thus improving the nucleophilicity of the now 'naked' acetate (Table 2).

Table 2. Results of nucleophilic substitution reactions to produce 4-ferrocenylbutyl acetate (**9**)



M = Li, Na, K

8a, X = Cl
8b, X = Br

9

Entry	Acetate (1 equiv)	Podand	Yield of 9 from 8a (%)	Yield of 9 from 8b (%)
1	LiOAc	**6a**	75	80
2	LiOAc	**7a**	69	73
3	LiOAc	**6c**	85	94
4	LiOAc	**7c**	67	76
5	NaOAc	**6a**	54	60
6	NaOAc	**7a**	49	53
7	NaOAc	**6c**	65	74
8	NaOAc	**7c**	50	56
9	KOAc	**6a**	38	44
10	KOAc	**7a**	26	32
11	KOAc	**6c**	45	53
12	KOAc	**7c**	35	40

Conclusions

The synthesis of some new 2,6-bis-substituted podands of 4*H*-pyran-4-one was reported. ^{1}H and ^{13}C NMR, FT-IR and mass spectrometry and CHN analysis were used to confirm the structure of synthesized compounds. To demonstrate the applicability of these podands in cation trapping processes, nucleophilic substituted reactions were carried out with various metal acetates. The use of lithium acetates gave better product yields than sodium or potassium acetates, presumably, owing to the superior complexation between the podand and the lithium cation.

Experimental Section

General. Commercial compounds were used without further purification. Column chromatography was performed using SiO_2 (60 Å, 230−400 mesh, particle size 0.040−0.063 mm) at 25 °C. ^{1}H and ^{13}C NMR spectra were obtained with Bruker FT-400 and 100 MHz spectrometers, respectively and the chemical shifts were reported in ppm and were referenced to the residual solvent as follows: $CHCl_3$ δ = 7.26 (^{1}H), δ = 76.0 (^{13}C). For ^{1}H NMR, coupling constants *J* were given in Hz and the resonance multiplicity was described as s (singlet), d (doublet), t (triplet), m (multiplet). The FT-IR spectra were reported with Bruker-Tensor 270 spectrometer. The mass spectra operated at 70 eV by Agilent (5975C VL) instrument, the most important peaks were reported in

m/z units with M^+ as the molecular ion. The Elemental analyses were carried out with an Elementor Vario EL. III instrument.

General procedure. Synthesis of dialkyl 4-oxo-4*H*-pyran-2, 6-carboxylates (4)

Trioxoheptanedioic acid dialkyl esters were prepared according to the procedure reported previously;[25] A mixture of the appropriate trioxoheptanedioic acid dialkyl ester **3** (0.13 mol) with the corresponding dry alcohol (300 mL) and concentrated hydrochloric acid (7 mL) was refluxed for 40 min. After that time the reaction mixture was cooled to r.t., filtered and the collected solid was further purified by recrystallization from alcohol.

Dimethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (4a). 3a (29.9 g, 0.13 mol) was used to give **4a** as pale brown needles (23.4 g, 85%). mp 114-115 °C (EtOH), lit. 115-116 °C.[28] IR (KBr, ν_{max}, cm^{-1}): 2998 (C-H, Aliphatic), 1750 (O-C=O), 1665 (C=O, pyran), 1556-1432 (C=C).

Diethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (4b). 3b (33.5 g, 0.13 mol) was used to give **4b** as pale brown solid (27.76 g, 89%). mp 61-62 °C (EtOH), lit. 60-62 °C.[29] IR (KBr, ν_{max}, cm^{-1}): 2985 (C-H, Aliphatic), 1751 (O-C=O), 1654 (C=O, pyran), 1534-1430 (C=C).

General procedure. Synthesis of mono and bis 4-oxo-4*H*-pyran-2,6-dicarboxylate derivatives 6a-d and 7a-h

Compound **4a** or **4b** (2.5 mmol), the appropriate glycol monoalkyl ether **5a-d** (7.5 mmol) and 2 drops of alkali metal methoxide catalyst (saturated solution in methanol) were combined in dry toluene (150 mL) in a flask equipped with a Soxhlet extraction apparatus. Molecular sieves (4 Å) were placed in the extraction thimble and the solution was refluxed for 48 h. Acetic acid (1 mL) was then added to neutralize the base. The reaction mixture was washed with water (2 × 30 mL) to remove excess of glycol derivatives. The organic layer was dried over $MgSO_4$ and concentrated in vacuum. The resulting crude oil was purified by column chromatography on silica gel with EtOAc/hexane (40:60) as eluent. Specific details are given for each compound.

The reaction of compound 4a with ethylene glycol monomethyl ether (5a). Dimethyl chelidonate (**4a**) (0.53 g, 2.5 mmol) and ethylene glycol monomethyl ether (**5a**) (0.57 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6a** and **7a** were obtained.

Bis(2-methoxyethyl) 4-oxo-4*H*-pyran-2,6-dicarboxylate (6a). Yellow oil (0.48 g, 64%, R_f = 0.80). IR (KBr, ν_{max}, cm^{-1}): 2931, 2885, 1760, 1662, 1402, 1379, 1348, 1274, 1202, 1116, 1028, 954, 779. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.42 (s, 6H, C**H**$_3$O-), 3.69-3.73 (4H, m, -C**H**$_2$OCH$_3$), 4.52-4.54 (4H, m, -COOC**H**$_2$-), 7.18 (2H, s, pyran-C**H**-3, 5-). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 60.3 (-O**C**H$_3$), 67.2 (-**C**H$_2$OCH$_3$), 71.0 (-COO**C**H$_2$-), 121.6 (pyran-**C**-3, -5), 153.9 (pyran-**C**-2, -6), 160.5 (-**C**OOCH$_2$-), 180.3 (pyran-**C**-4). MS: *m/z* 300 (M^+). Anal. calcd. for $C_{13}H_{16}O_8$: C, 52.00%; H, 5.37%. Found: C, 51.80%; H, 5.25%.

2-(2-Methoxyethyl) 6-methyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7a). Yellow oil (0.10 g, 16%, R_f = 0.61). IR (KBr, ν_{max}, cm^{-1}): 2993, 2895, 1743, 1660, 1400, 1375, 1352, 1277, 1114, 750. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.42 (s, 3H, C**H**3O-), 3.70-3.73 (2H, m, -C**H**$_2$OCH$_3$), 4.00 (3H, s, C**H**$_3$OCO-), 4.50-4.54 (2H, m, -COOC**H**$_2$-), 7.17 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 59.1 (**C**H$_3$OCH$_2$-), 68.2 (-COOCH$_2$**C**H$_2$-), 70.8 (-COO**C**H$_3$), 71.1 (-COO**C**H$_2$CH$_2$-), 120.1 (pyran-**C**-5), 120.4 (pyran-**C**-3), 152.6 (pyran-**C**-6), 153.7 (pyran-**C**-2), 159.3 (-**C**OOCH$_3$), 160.3 (-**C**OOCH$_2$CH$_2$-), 180.1 (pyran-**C**-4). MS: *m/z* 256 (M^+). Anal. calcd. for $C_{11}H_{12}O_7$: C, 51.57%; H, 4.72%. Found: C, 51.42%; H, 4.68%.

Reaction of compound 4b with ethylene glycol monomethyl ether (5a)

Diethyl chelidonate (**4b**) (0.60 g, 2.5 mmol) and ethylene glycol monomethyl ether (**5a**) (0.57 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6a** and **7e** were obtained.

Bis(2-methoxyethyl) 4-oxo-4*H*-pyran-2,6-dicarboxylate (6a). Yellow oil (0.52 g, 69%) was obtained. The spectral properties were identical to that of compound **6a** reported earlier (see Section 2.1.1.).**2-(2-**

Methoxyethyl) 6-ethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7e). Yellow oil (0.12 g, 19%, R_f = 0.51). IR (KBr, ν_{max}, cm^{-1}): 2995, 2893, 1752, 1665, 1410, 1378, 1348, 1265, 1138, 765. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (3H, t, $^3J_{HH}$ 6.5 Hz, -OCH_2CH_3), 3.41 (3H, s, -OCH_2CH_3), 3.71-3.74 (2H, m, -CH_2OCH_3), 4.21 (2H, q, $^3J_{HH}$ 6.5 Hz, CH_3CH_2OCO-), 4.48-4.52 (2H, m, -$COOCH_2$-), 7.15 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 13.8 (-$COOCH_2CH_3$), 59.4 (CH_3OCH_2-), 61.0 (-$COOCH_2CH_3$), 68.1 (-$COOCH_2CH_2$-), 71.1 (-$COOCH_2CH_2$), 120.0 (pyran-**C**-5), 120.3 (pyran-**C**-3), 152.5 (pyran-**C**-6), 153.6 (pyran-**C**-2), 159.2 (-$COOC_2H_5$), 160.1 (-$COOCH_2CH_2$-), 180.1 (pyran-**C**-4). MS: *m/z* 270 (M^+). Anal. calcd. for $C_{12}H_{14}O_7$: C, 53.34%; H, 5.22%. Found: C, 53.23%; H, 5.13%.

Reaction of compound 4a with ethylene glycol monomethyl ether (5b)

Diethyl chelidonate (**4a**) (0.53 g, 2.5 mmol) and ethylene glycol monomethyl ether (**5b**) (0.68 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6b** and **7b** were obtained.

Bis(2-ethoxyethyl) 4-oxo-4*H*-pyran-2,6-dicarboxylate (6b). Yellow oil (0.50 g, 61%, R_f = 0.75). IR (KBr, ν_{max}, cm^{-1}): 2937, 2887, 1757, 1665, 1412, 1373, 1342, 1267, 1215, 1130, 1035, 962, 765. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.22 (3H, s, $^3J_{HH}$ 7 Hz, -OCH_2CH_3), 3.43 (2H, q, $^3J_{HH}$ 7 Hz, CH_3CH_2O-Å), 3.71-3.75 (4H, m, -$CH_2OC_2H_5$), 4.48-4.53 (4H, m, -$COOCH_2$-), 7.2 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 15.1 (-OCH_2CH_3), 66.1 (-OCH_2CH_3), 67.1 (-$COOCH_2CH_2$-), 71.1 (-$COOCH_2CH_2$-), 121.5 (pyran-**C**-3, -5), 154.0 (pyran-**C**-2, -6), 160.3 (-$COOCH_2CH_2$), 180.2 (pyran-**C**-4). MS: *m/z* 328 (M^+). Anal. calcd. for $C_{15}H_{20}O_8$: C, 54.88%; H, 6.14%. Found: C, 54.75%; H, 5.98%.

2-(2-Ethoxyethyl) 6-methyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7b). Yellow oil (0.09 g, 14%, R_f = 0.57). IR (KBr, ν_{max}, cm^{-1}): 2989, 2887, 1754, 1663, 1408, 1372, 1347, 1273, 1120, 762. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.22 (3H, t, *J* = 7 Hz, OCH_2CH_3), 3.41 (2H, q, *J* = 7 Hz, -OCH_2CH_3), 3.70-3.74 (2H, m, -$CH_2OC_2H_5$), 4.01 (3H, s, -$COOCH_3$), 4.50-4.53 (2H, m, -$COOCH_2$-), 7.19 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 15.0 (-$CH_2OCH_2CH_3$), 66.2 (-$CH_2OCH_2CH_3$), 68.1 (-$COOCH_2CH_2$-), 70.3 (-$COOCH_3$), 71.2 (-$COOCH_2CH_2$-), 120.1 (pyran-**C**-5), 120.3 (pyran-**C**-3), 152.5 (pyran-**C**-6), 153.6 (pyran-**C**-2), 159.2 (-$COOCH_3$), 160.1 (-$COOCH_2CH_2$-), 179.9 (pyran-**C**-4). MS: *m/z* 270 (M^+). Anal. calcd. for $C_{12}H_{14}O_7$: C, 53.34%; H, 5.22%. Found: C, 53.25%; H, 5.16%.

Reaction of compound 4b with ethylene glycol monomethyl ether (5b)

Diethyl chelidonate (**4b**) (0.60 g, 2.5 mmol) and ethylene glycol monomethyl ether (**5b**) (0.68 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6b** and **7f** were obtained.

Bis(2-ethoxyethyl) 4-oxo-4*H*-pyran-2,6-dicarboxylate (6b). Yellow oil (0.55 g, 67%) was obtained; The spectral properties were identical to that of compound **6b** reported earlier (see Section 2.3.1.).

2-(2-Ethoxyethyl) 6-ethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7f). Yellow oil (0.08 g, 11%, R_f = 0.49). IR (KBr, ν_{max}, cm^{-1}): 2991, 2887, 1739, 1661, 1401, 1371, 1340, 1251, 1145, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.21 (3H, t, $^3J_{HH}$ 7 Hz, -OCH_2CH_3), 1.29 (3H, t, $^3J_{HH}$ 6.5 Hz, -$COOCH_2CH_3$), 3.43 (2H, q, $^3J_{HH}$ 7 Hz, -OCH_2CH_3), 3.69-3.72 (2H, m, -$CH_2OC_2H_5$), 4.22 (2H, q, $^3J_{HH}$ 6.5 Hz, -$COOCH_2CH_3$), 4.49-4.53 (2H, m, -$COOCH_2$-), 7.17 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 13.9 (-$COOCH_2CH_3$), 15.1 (-$CH_2OCH_2CH_3$), 60.9 (-$COOCH_2CH_3$), 65.9 (-$CH_2OCH_2CH_3$), 68.0 (-$COOCH_2CH_2$-), 71.2 (-$COOCH_2CH_2$-), 120.1 (pyran-**C**-5), 120.3 (pyran-**C**-3), 152.3 (pyran-**C**-6), 153.5 (pyran-**C**-2), 160.0 (-$COOC_2H_5$), 160.2 (-$COOCH_2CH_2$-), 178.0 (pyran-**C**-4). MS: *m/z* 284 (M^+). Anal. calcd. for $C_{13}H_{16}O_7$: C, 54.93%; H, 5.67%. Found: C, 54.81%; H, 5.53%.

Reaction of compound 4a with diethylene glycol monomethyl ether (5c)

Diethyl chelidonate (**4a**) (0.53 g, 2.5 mmol) and diethylene glycol monomethyl ether (**5c**) (0.90 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6c** and **7c** were obtained.

Bis[2-(2-methoxyethoxy)ethyl] 4-oxo-4*H*-pyran-2,6-dicarboxylate (6c). Yellow oil (0.70 g, 72%, R_f = 0.70). IR (KBr, ν_{max}, cm^{-1}): 2985, 2883, 1755, 1660, 1623, 1598, 1456, 1275, 1248, 1109, 956, 862, 779. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.38 (6H, s, CH_3O-), 3.51-3.56 (4H, m, -$CH_2CH_2OCH_3$), 3.68-3.71 (4H, m, -$CH_2CH_2OCH_3$), 3.80-3.85 (4H, m, -$COOCH_2OCH_2$-), 4.52-4.55 (4H, m, -$COOCH_2$-), 7.18 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz,

$CDCl_3$): δ_C 59.0 (-CH_2O**C**H_3), 66.0 (-CH_2**C**H_2OCH_3), 68.5 (-**C**$H_2CH_2OCH_3$), 70.6 (-$COOCH_2$**C**H_2-), 71.8 (-COO**C**H_2CH_2-), 120.3 (pyran-**C**-3, -5), 152.7 (pyran-**C**-2, -6), 159.2 (-**C**$OOCH_2CH_2$), 179.1 (pyran-**C**-4). MS: *m/z* 388 (M^+). Anal. calcd. for $C_{17}H_{24}O_{10}$: C, 52.58%; H, 6.22%. Found: C, 52.45%; H, 6.13%.

2-[2-(2-Methoxyethoxy)ethyl] 6-methyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7c). Yellow oil (0.07 g, 9%, R_f = 0.38). IR (KBr, ν_{max}, cm^{-1}): 2957, 2827, 1760, 1661, 1627, 1441, 1408, 1352, 1279, 1252, 1111, 955, 889, 781. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.38 (3H, s, C**H**$_3$O-), 3.56-3.59 (2H, m, -C**H**$_2CH_2OCH_3$), 3.64-3.68 (2H, m, -CH_2C**H**$_2OCH_3$), 3.84-3.88 (2H, m, -$COOCH_2$C**H**$_2$-), 4.00 (3H, s, -COOC**H**$_3$), 4.54-4.58 (2H, m, -COOC**H**$_2$-), 7.17 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 53.6 (-CH_2O**C**H_3), 58.9 (-CH_2**C**H_2OCH_3), 66.0 (-**C**$H_2CH_2OCH_3$), 68.4 (-$COOCH_2$**C**H_2-), 70.5 (-COO**C**H_3), 71.7 (-COO**C**H_2CH_2-), 120.1 (pyran-**C**-5), 120.2 (pyran-**C**-3), 152.6 (pyran-**C**-6), 152.7 (pyran-**C**-2), 159.2 (-$COOCH_3$), 159.7 (-$COOCH_2CH_2$-), 178.9 (pyran-**C**-4). MS: *m/z* 300 (M^+). Anal. calcd. for $C_{13}H_{16}O_8$: C, 52.00%; H, 5.37%. Found: C, 51.82%; H, 5.24%.

Reaction of compound 4b with diethylene glycol monomethyl ether (5c)

Diethyl chelidonate (**4b**) (0.60 g, 2.5 mmol) and diethylene glycol monomethyl ether (**5c**) (0.90 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6c** and **7g** were obtained.

Bis[2-(2-methoxyethoxy)ethyl] 4-oxo-4*H*-pyran-2,6-dicarboxylate (6c). Yellow oil (0.67 g, 70%) was obtained; The spectral properties were identical to that of compound **6c** reported earlier (see Section 2.5.1.).

2-[2-(2-Methoxyethoxy)ethyl] 6-ethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7g). Yellow oil (0.10 g, 13%, R_f = 0.43). IR (KBr, ν_{max}, cm^{-1}): 2962, 2835, 1775, 1665, 1632, 1445, 1401, 1364, 1259, 1257, 1109, 962, 884, 793. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (3H, t, $^3J_{HH}$ 6.5 Hz, -$COOCH_2$C**H**$_3$), 3.37 (3H, s, C**H**$_3$O-), 3.64-3.68 (4H, m, -OC**H**$_2$C**H**$_2OCH_3$), 3.81-3.86 (2H, m, -$COOCH_2$C**H**$_2$O-), 4.22 (2H, q, $^3J_{HH}$ 6.5 Hz, -COOC**H**$_2CH_3$), 4.50-4.54 (2H, m, -COOC**H**$_2$-), 7.16 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 13.8 (-$COOCH_2$**C**H_3), 53.5 (-CH_2O**C**H_3), 58.8 (-CH_2**C**H_2OCH_3), 61.3 (-COO**C**H_2CH_3), 66.0 (-**C**$H_2CH_2OCH_3$), 68.2 (-$COOCH_2$**C**H_2-), 71.3 (-COO**C**H_2CH_2-), 120.04 (pyran-**C**-5), 120.15 (pyran-**C**-3), 152.4 (pyran-**C**-6), 152.6 (pyran-**C**-2), 159.9 (-**C**OOC_2H_5), 160.0 (-**C**$OOCH_2$-), 179.8 (pyran-**C**-4). MS: *m/z* 314 (M^+). Anal. calcd. for $C_{14}H_{18}O_8$: C, 53.50%; H, 5.77%. Found: C, 53.39%; H, 5.62%.

Reaction of compound 4a with diethylene glycol monoethyl ether (5d)

Diethyl chelidonate (**4a**) (0.53 g, 2.5 mmol) and diethylene glycol monoethyl ether (**5d**) (0.10 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6d** and **7d** were obtained.

Bis[2-(2-ethoxyethoxy)ethyl] 4-oxo-4*H*-pyran-2,6-dicarboxylate (6d). Yellow oil (0.68 g, 65%, R_f = 0.64). IR (KBr, ν_{max}, cm^{-1}): 2924, 2883, 1749, 1662, 1458, 1385, 1350, 1269, 1242, 1111, 1030, 953, 862, 777. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.11 (6H, t, $^3J_{HH}$ 7 Hz, -OCH_2C**H**$_3$), 3.44 (4H, q, $^3J_{HH}$ 7 Hz, -OC**H**$_2CH_3$), 3.60-3.64 (8H, m, -C**H**$_2$C**H**$_2OC_2H_5$), 3.73-3.76 (4H, m, -$COOCH_2OCH_2$-), 4.43-4.48 (4H, m, -COOC**H**$_2$-), 7.07 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 15.1 (-CH_2OCH_2**C**H_3), 65.2 (-CH_2O**C**H_2CH_3), 66.0 (-CH_2**C**$H_2OC_2H_5$), 68.3 (-**C**$H_2CH_2OC_2H_5$), 70.3 (-$COOCH_2$**C**H_2-), 71.7 (-COO**C**H_2CH_2-), 120.2 (pyran-**C**-3, -5), 152.6 (pyran-**C**-2, -6), 159.1 (-**C**$OOCH_2CH_2$-), 179.0 (pyran-**C**-4). MS: *m/z* 416 (M^+). Anal. calcd. for $C_{19}H_{28}O_{10}$: C, 54.80%; H, 6.78%. Found: C, 54.68%; H, 6.62%.

2-[2-(2-Ethoxyethoxy)ethyl] 6-methyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7d). Yellow oil (0.08 g, 10%, R_f = 0.40). IR (KBr, ν_{max}, cm^{-1}): 2957, 2893, 1760, 1670, 1627, 1598, 1445, 1440, 1377, 1350, 1277, 1250, 1120, 955, 889, 781. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.21 (3H, q, $^3J_{HH}$ 7 Hz, -OCH_2C**H**$_3$), 3.54 (2H, q, $^3J_{HH}$ 7 Hz, -OC**H**$_2CH_3$), 3.63-3.67 (4H, m, -C**H**$_2$C**H**$_2OC_2H_5$), 3.82-3.85 (2H, m, -$COOCH_2$C**H**$_2$-), 4.00 (3H, s, -COOC**H**$_3$), 4.51-4.55 (2H, m, -COOC**H**$_2$-), 7.17 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 15.1 (-OCH_2**C**H_3), 59.1 (-**C**$H_2OC_2H_5$), 65.8 (-CH_2O**C**H_2CH_3), 66.0 (-**C**$H_2CH_2OC_2H_5$), 68.6 (-$COOCH_2$**C**H_2-), 70.6 (-COO**C**H_3), 71.8 (-COO**C**H_2CH_2-), 120.25 (pyran-**C**-5), 120.34 (pyran-**C**-3), 152.6 (pyran-**C**-6), 152.7 (pyran-**C**-2), 159.3 (-**C**$OOCH_3$), 159.8 (-**C**$OOCH_2CH_2$-),

179.1 (pyran-**C**-4). MS: *m/z* 314 (M^+). Anal. calcd. for $C_{14}H_{18}O_8$: C, 53.50%; H, 5.77%. Found: C, 53.39%; H, 5.62%.

Reaction of compound 4b with diethylene glycol monoethyl ether (5d)

Diethyl chelidonate (**4b**) (0.60 g, 2.5 mmol) and diethylene glycol monoethyl ether (**5d**) (0.10 g, 7.5 mmol) were reacted according to the general procedure. Compounds **6d** and **7h** were obtained.

Bis[2-(2-ethoxyethoxy)ethyl] 4-oxo-4*H*-pyran-2,6-dicarboxylate (6d). Yellow oil (0.72 g, 69%) was obtained; The spectral properties were identical to that of compound **6d** reported earlier. (see section **2.7.1.**)

2-[2-(2-Ethoxyethoxy)ethyl] 6-ethyl 4-oxo-4*H*-pyran-2,6-dicarboxylate (7h). Yellow oil (0.09 g, 11%, R_f = 0.34). IR (KBr, ν_{max}, cm^{-1}): 2968, 2839, 1770, 1651, 1639, 1451, 1410, 1369, 1271, 1248, 1115, 975, 889, 787. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.21 (3H, t, $^3J_{HH}$ 7 Hz, -$OCH_2C\mathbf{H}_3$), 1.30 (3H, t, $^3J_{HH}$ 6.5 Hz, -$COOCH_2C\mathbf{H}_3$), 3.42 (2H, q, $^3J_{HH}$ 7 Hz, -$OC\mathbf{H}_2CH_3$), 3.65-3.69 (4H, m, -$C\mathbf{H}_2C\mathbf{H}_2OC_2H_5$), 3.80-3.85 (2H, m, -$COOCH_2C\mathbf{H}_2$-), 4.21 (2H, q, $^3J_{HH}$ 6.5 Hz, -$COOC\mathbf{H}_2CH_3$), 4.50-4.55 (2H, m, -$COOC\mathbf{H}_2$-), 7.15 (2H, s, pyran-C**H**-3, -5). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 13.4 (-$COOCH_2\mathbf{C}H_3$), 15.2 (-$CH_2OCH_2\mathbf{C}H_3$), 58.6 (-$\mathbf{C}H_2OC_2H_5$), 61.5 (-$COO\mathbf{C}H_2CH_3$), 65.6 (-$CH_2O\mathbf{C}H_2CH_3$), 66.0 (-$\mathbf{C}H_2CH_2OC_2H_5$), 68.4 (-$COOCH_2\mathbf{C}H_2$-), 71.1 (-$COO\mathbf{C}H_2CH_2$), 120.1 (pyran-**C**-5), 120.3 (pyran-**C**-3), 152.2 (pyran-**C**-6), 152.8 (pyran-**C**-2), 159.82 (-$\mathbf{C}OOC_2H_5$), 160.01 (-$\mathbf{C}OOCH_2$-), 180.3 (pyran-**C**-4). MS: *m/z* 328 (M^+). Anal. calcd. for $C_{15}H_{20}O_8$: C, 54.88%; H, 6.14%. Found: C, 54.71%; H, 6.01%.

Synthesis of 4-chlorobutyl ferrocene (8a). 8a was prepared according to a literature procedure.[26] Dark orange oil (1.25 g, 90%) was obtained. IR (KBr, ν_{max}, cm^{-1}): 3081, 2929, 1695, 1466, 1093, 1010, 660, 487. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.63-1.69 (2H, m, C$\mathbf{H}_2$), 1.77–1.84 (2H, m, C$\mathbf{H}_2$), 2.36 (2H, t, Cp–C$\mathbf{H}_2$), 3.55 (2H, t, C$\mathbf{H}_2$–Cl), 4.03-4.09 (4H, m, Cp), 4.11 (5H, s, Cp).

Synthesis of 4-bromobutyl ferrocene (8b). 8b was prepared according to a literature procedure.[27] Brown oil (1.45 g, 85%) was obtained. IR (KBr, ν_{max}, cm^{-1}): 3090, 2928, 1684, 1454, 1103, 1000, 815, 485. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.62–1.69 (2H, m, C$\mathbf{H}_2$), 1.85–1.92 (2H, m, C$\mathbf{H}_2$), 2.36 (2H, t, Cp–C$\mathbf{H}_2$), 3.42 (2H, t, C$\mathbf{H}_2$–Br), 4.02-4.08 (4H, m, Cp), 4.10 (5H, s, Cp).

General procedure. Synthesis of 4-ferrocenylbutyl acetate (9) in the presence of different podands

Compound **8a** or **8b** (0.36 mmol) was dissolved in acetonitrile (4 mL) in a flask equipped with a reflux condenser and magnetic stirrer and to this, a solution of the appropriate acetate salt (0.36 mmol) and podand **6a-d** or **7a-h** (0.012 mmol) in acetonitrile (1 mL), was added. The solution was refluxed for 24 h. After completion of the reaction, monitored by TLC, the solvents were removed under reduced pressure. The residue was extracted with dichloromethane (3 × 10 mL) and washed with water (20 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuum. The resulting orange oil was purified by column chromatography on silica gel with EtOAc/hexane (10:90) as eluent. Specific yields are given for each compound in Table 2.

4-Ferrocenylbutyl acetate (**9**) was obtained as orange oil. IR (KBr, ν_{max}, cm^{-1}): 2924, 2891, 2868, 1740, 1550, 1465, 1202, 954, 514. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.55-1.59 (2H, m, C$\mathbf{H}_2$), 1.65-1.69 (2H, m, C$\mathbf{H}_2$), 2.05 (3H, s, C$\mathbf{H}_3$), 2.32 (2H, t, Cp-C$\mathbf{H}_2$), 4.05-4.18 (11H, m, C$\mathbf{H}_2$-O, and Cp). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 19.9 (**C**H_3), 26.2 (CH_2), 27.2 (CH_2), 28.0 (CH_2), 62.7 (**C**H_2-O), 66.4 (Cp), 67.39 (Cp), 67.89 (Cp), 88.2 (Cp-CH_2), 170.0 (C=O). MS: *m/z* 300 (M^+). Anal. calcd. for $C_{16}H_{20}FeO_2$: C, 64.01%; H, 6.71%. Found: C, 64.12%; H, 6.78%.

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