Supporting Information

Cu(I)-Catalyzed Domino Reactions: Efficient and Selective Synthesis of 4*H*-Chromenes and Naphthalenes

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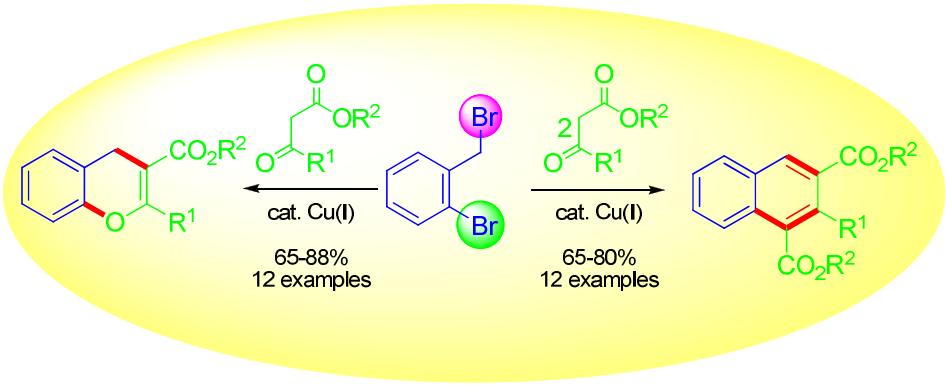
Graphical Abstract



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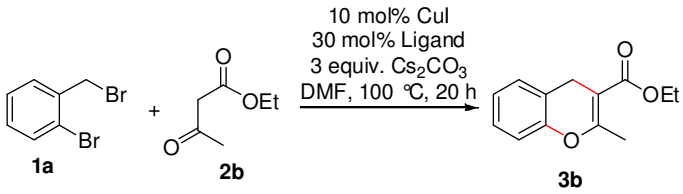
1. General methods

All starting materials were purchased from commercial suppliers (Sigma-Aldrich Chemical Co., Acros Organics, Lancaster Organics) and 2-bromobenzyl bromide was used without further purification. β-Ketoesters were freshly distilled over $MgSO_4$ prior to use. All reactions were carried out under an argon atmosphere in oven-dried glassware with magnetic stirring. Temperatures are reported as inner temperatures. Solvents used in extraction and purification were distilled prior to use. Thin-layer chromatography (TLC) was performed on Alugram SIL G/UV $_{254}$ (Macherey and Nagel). Compounds were visualized with UV light (λ = 254 nm) and/or by immersion in an ethanolic vanillin solution followed by heating. Products were purified by flash chromatography on silica gel 60 M, 230 - 400 mesh (Macherey & Nagel). Melting points were determined on a Büchi melting point apparatus B-545 with open capillary tubes and are uncorrected. IR spectra were measured on a Perkin-Elmer Spectrum One (FT-IR-spectrometer). UV/VIS spectra were recorded with a Varian Cary 50. ^{1}H (^{13}C) NMR spectra were recorded at 300 (75) MHz on a Varian ^{Unity}Inova spectrometer using $CDCl_3$ and DMSO as solvent. The ^{1}H and ^{13}C chemical shifts were referenced to residual solvent signals at $\delta_{H/C}$ 7.26 /77.00 ($CDCl_3$) and $\delta_{H/C}$ 2.50 /39.50 (DMSO) relative to TMS as internal standards. HSQC-, HMBC- and COSY-spectra were recorded on a Varian ^{Unity}Inova at 300 MHz. Coupling constants *J* [Hz] were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Low-resolution electron impact mass spectra (EI-LRMS) and exact mass electron impact mass spectra (HRMS) were obtained at 70 eV on a Finnigan MAT 95 instrument. Gas-chromatography mass spectra (GC-MS) were done on a Thermo Polaris Q equipped with a Varian Trace GC Ultra and a column DB5 (TGC / 50 / 5 / 10 / 280). The intensities are reported as percentages relative to the base peak after the corresponding *m/z* value. Elemental analyses were obtained from the Institut für Organische Chemie der Universität Stuttgart.

2. Optimization of the Cu(I)-catalyzed synthesis of 4*H*-chromenes

Table 1. Variation of the ligands for the Cu(I)-catalyzed synthesis of **3b**.[a, b]

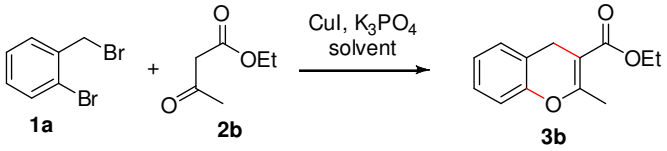


1a **2b** **3b**

entry	ligand	yield **3b** [%]
1	L-proline	46
2	*trans*-4-hydroxy-L-proline	55
3	*N,N*-dimethylglycine	35
4	*tris*-(2-aminoethyl)amine	39
5	TMEDA	61
6	DMEDA	55
7	*1,10*-phenanthroline	52
8	*2,2'*-dipyridyl	35

[a]All reactions were performed in sealed vials. [b]1 mmol of **1a** was reacted with 1 mmol of **2b**.

Table 2. Variation of solvent, reaction time and reaction temperature for the synthesis of **3b**.[a, b]

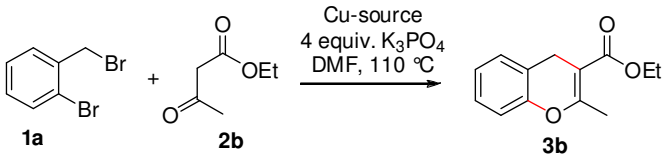


1a **2b** **3b**

entry	CuI [equiv.]	K_3PO_4 [equiv.]	solvent	T [°C]	*t* [h]	yield **3b** [%]
1	0.1	3	DMF	100	20	60
2	0.1	3	DMF	100	20	64
3	0.1	4	DMF	100	20	66
4	0.2	4	DMF	110	20	71
5	0.2	4	DMF	110	22	74
6	0.2	4	DMF	110	22	64[c]
7	0.2	4	DMA	110	22	75
8	0.2	4	DMF	120	22	70
9	0.2	4	DMF	110	24	76
10	0.2	4	DMA	110	24	76

[a]The reactions were performed in sealed vials. [b]1 mmol of **1a** was reacted with 1 mmol of **2b**. [c]The reaction was performed in a round-bottomed flask equipped with a reflux condenser under argon.

Table 3. Variation of the amount of CuI and Cu-sources.[a, b]



Entry	Cu-source	Equiv.	t [h]	Yield **3b** [%]
1	-	-	20	-
2	CuI (98%)	0.01	20	25
3	CuI	0.05	20	55
4	CuI	0.1	20	67
5	CuI	0.15	20	69
6	CuI	0.2	20	71
7	CuI	0.2	24	76
8	CuI (99.999%)	0.2	24	73
9	CuBr	0.2	24	56
10	CuCl	0.2	24	39
11	$CuOTf.(CH_3CN)_4$	0.2	24	51
12	$Cu(acac)_2$	0.2	24	34
13	$Cu(OAc)_2$	0.2	24	36
14	Cu	0.2	22	22

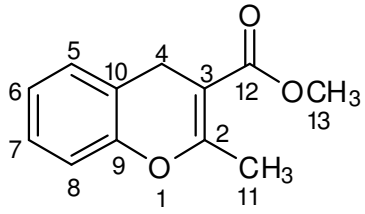
[a]All reactions were performed in sealed vials. [b]1 mmol of **1a** was reacted with 2 mmol of **2b**.

3. General experimental procedure I for the Cu(I)-catalyzed synthesis of 4*H*-chromenes

An oven-dried 10 mL vial was charged with 39 mg (0.2 mmol) CuI (98%), 875 mg (4.0 mmol) potassium phosphate (97%), 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**) and 1.0 - 2.0 mmol freshly distilled β-keto ester **2** under air. The vial was sealed, evacuated and backfilled with argon (six times), then 3 mL freshly distilled dry DMF were added. The reaction mixture was stirred at 110 °C until the 2-bromobenzyl bromide was consumed (TLC). After cooling to room temperature the reaction mixture was partitioned between 50 mL EtOAc and 20 mL saturated brine. The aqueous phase was extracted with EtOAc (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The residue thus obtained was purified by flash column chromatography over silica gel (cyclohexane/EtOAc = 70:2, unless otherwise indicated).

4. Synthesis and characterization of 4*H*-chromenes 3a-k, 5

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-methyl ester (3a)[1]

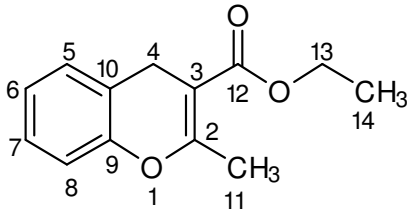


3a

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 232 mg (2.0 mmol) methyl acetoacetate (**2a**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 149 mg (73%) 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-methyl ester (**3a**) as a colourless solid.

M.**p**. 40−42 °C; $\boldsymbol{R_f}$ = 0.70 (cyclohexane/EtOAc = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.38 (s, 3H; 11-H_3), 3.69 (s, 2H; 4-H_2), 3.77 (s, 3H; 13-H_3), 6.90 (dd, ^3J (7-H, 8-H) = 8.1 Hz, ^4J (6-H, 8-H) = 1.2 Hz, 1H; 8-H), 7.00 (ddd, ^3J (5-H, 6-H) = 7.5 Hz, ^3J (6-H, 7-H) = 6.8 Hz, ^4J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.09 (br d, ^3J (5-H, 6-H) = 8.0 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^3J (7-H, 8-H) = 8.1 Hz, ^3J (6-H, 7-H) = 7.1 Hz, ^4J (5-H, 7-H) = 1.9 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.3 (C-11), 24.8 (C-4), 51.4 (C-13), 100.7 (C-3), 116.0 (C-8), 120.5 (C-10), 124.1 (C-6), 127.5 (C-7), 128.8 (C-5), 150.1 (C-9), 160.9 (C-2), 168.1 ppm (C-12); **MS** (GC-MS): *m/z* (%) = 204 (19) [M^+] 189 (100) [$M-CH_3$]$^+$, 171 (30) [189–H_2O]$^+$, 145 (30) [$C_{10}H_9O$]$^+$, 115 (40) [C_9H_7]$^+$, 91 (10) [C_7H_7]$^+$.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-ethyl ester (3b)[1]

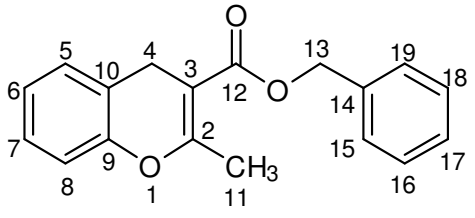


3b

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 260 mg (2.0 mmol) ethyl acetoacetate (**2b**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 165 mg (76%) 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-ethyl ester (**3b**) as a colourless solid.

M.p. 40−41 °C (ref.[1] 39−41 °C); $\boldsymbol{R_f}$ = 0.72 (cyclohexane/EtOAc = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.33 (t, ^3J (13-H, 14-H) = 7.2 Hz, 3H; 14-H_3), 2.38 (s, 3H; 11-H_3), 3.60 (s, 2H; 4-H_2), 4.23 (q, ^3J (13-H, 14-H) = 6.9 Hz, 2H; 13-H), 6.90 (dd, ^3J (7-H, 8-H) = 8.1 Hz, ^4J (6-H, 8-H) = 1.3 Hz, 1H; 8-H), 7.01 (ddd, ^3J (5-H, 6-H) = 7.6 Hz, ^3J (6-H, 7-H) = 6.8 Hz, ^4J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.09 (br d, ^3J (5-H, 6-H) = 8.0 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^3J (7-H, 8-H) = 8.1 Hz, ^3J (6-H, 7-H) = 7.1, ^4J (5-H, 7-H) = 1.9 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.4 (C-11), 19.3 (C-14), 24.8 (C-4), 60.1 (C-13), 100.9 (C-3), 116.0 (C-8), 120.5 (C-10), 124.0 (C-6), 127.5 (C-7), 128.8 (C-5), 150.2 (C-9), 160.6 (C-2), 167.7 ppm (C-12); **MS** (GC-MS): *m/z* (%) = 218 (10) [M^+], 189 (100) [$M-C_2H_5]^+$, 173 (12) $[C_{11}H_9O_2]^+$, 145 (14) $[C_{10}H_9O]^+$, 115 (31) $[C_9H_7]^+$, 91 (9) $[C_7H_7]^+$, 77 (7) $[C_6H_5]^+$, 51 (5) $[C_4H_3]^+$.

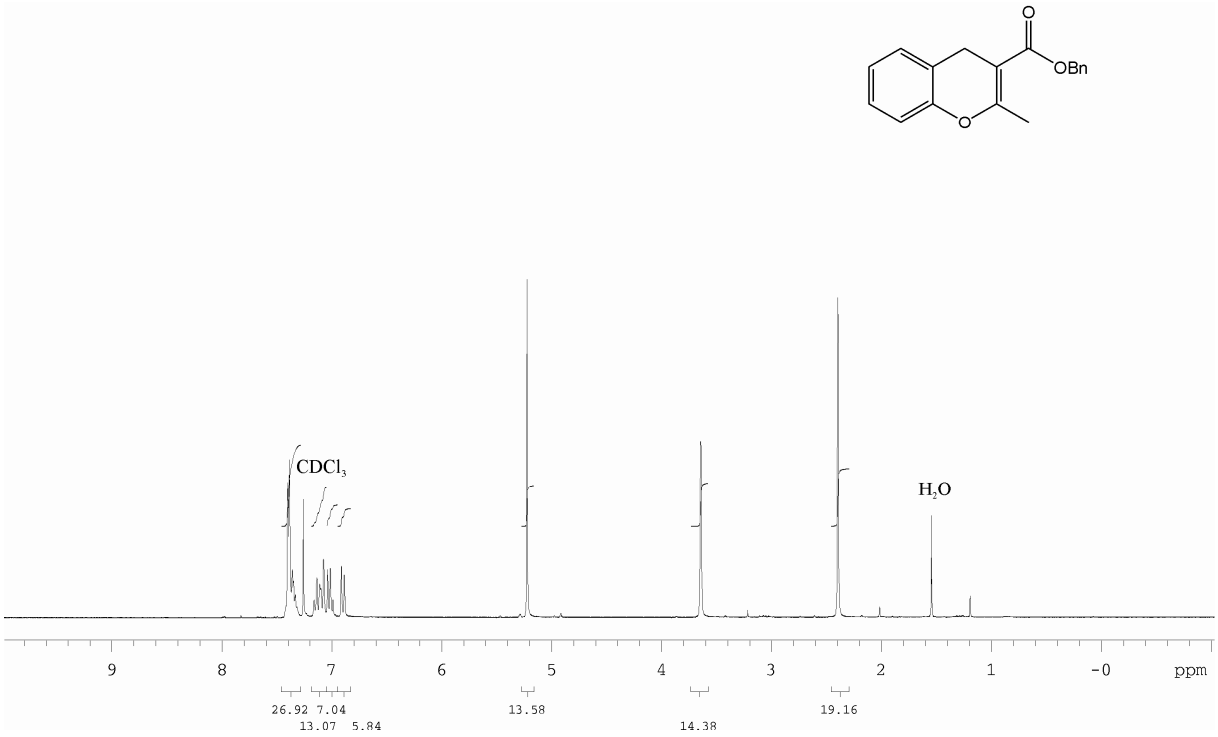
Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-benzyl ester (3c)



3c

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 384 mg (2.0 mmol) benzyl acetoacetate (**2c**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were

reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 207 mg (74%) 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-benzyl ester (**3c**) as a colourless oil.



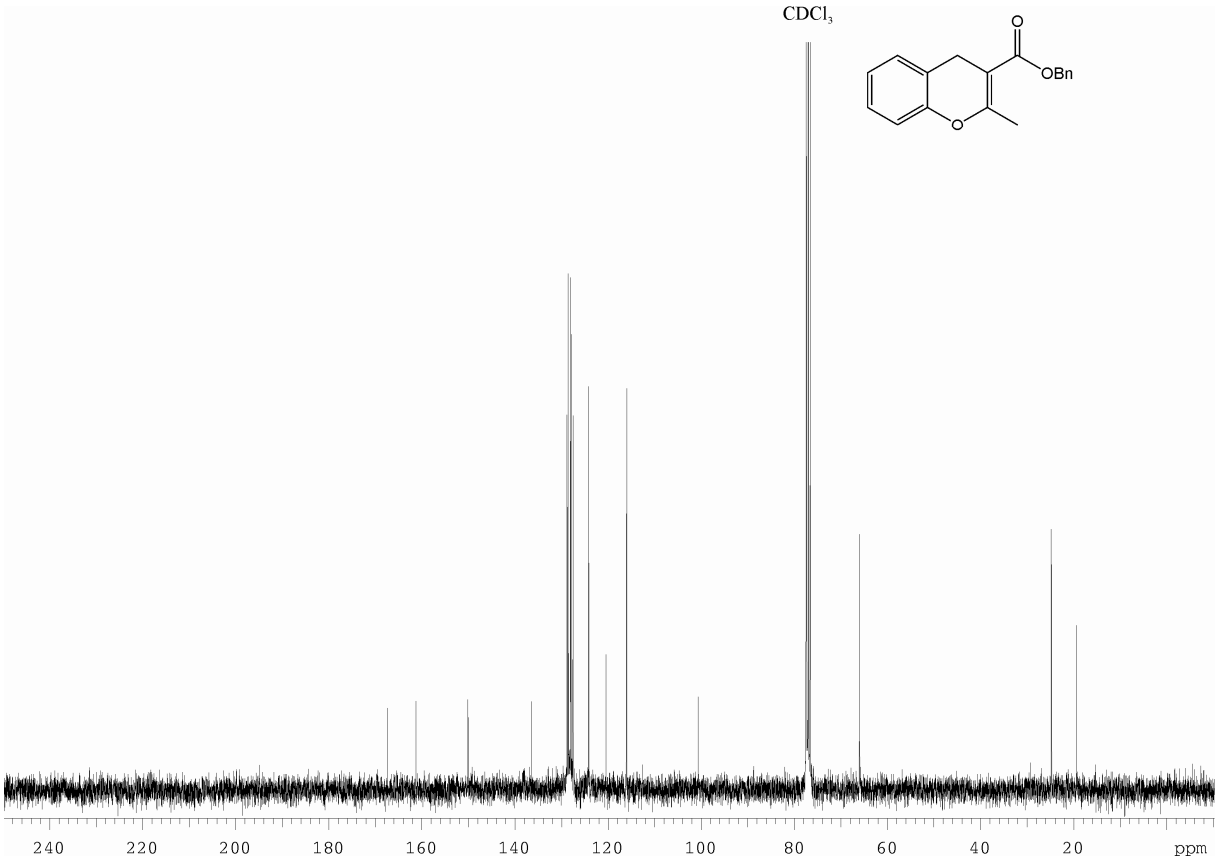
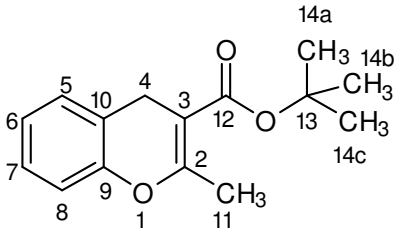


Figure 1. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3c** in $CDCl_3$.

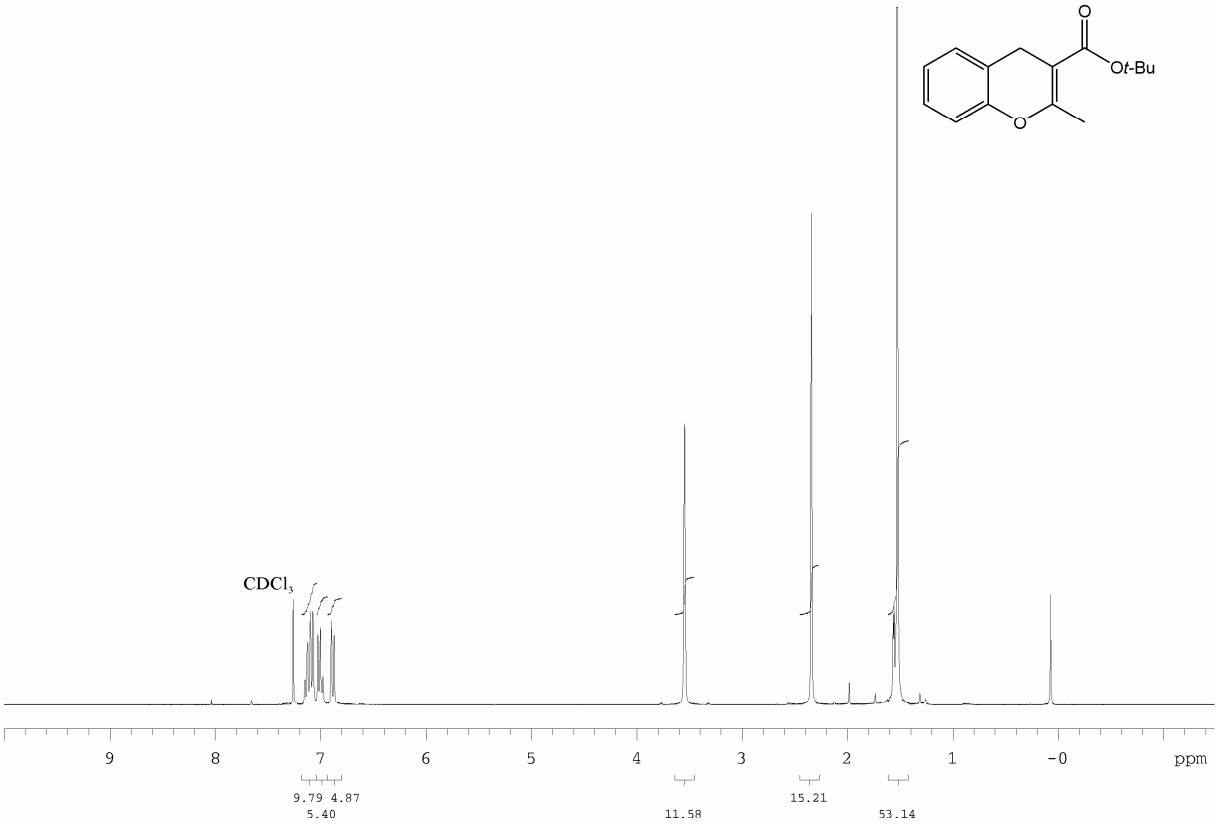
$\boldsymbol{R_f}$ = 0.70 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3033 (w; CH_2, CH_3), 1711 (s; C=O), 1644 (s; alkene C=C), 1586 (m; arom. C=C), 1490 (m; arom. C=C), 1457 (m; alkane C-H), 1381(m; alkane C-H), 1287 (s; ester C-O), 1251 (s; ether C-O), 1186 (s), 1138 (m), 1103 (s), 1052 (s), 1028 (s), 984 (s), 868 (m; arom. C-H), 750 (s; alkane C-H), 695 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 280 (3.97), 332 nm (3.29); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.40 (t, ^{2}J (11-H, 11-H) = 1.4 Hz, 3H; 11-H_3), 3.64 (br s, 2H; 4-H_2), 5.23 (br s, 2H; 13-H_2), 6.90 (dd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 8-H), 7.02 (ddd, ^{3}J (5-H, 6-H) = 7.6 Hz, ^{3}J (6-H, 7-H) = 6.9 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.09 (br d, ^{3}J (5-H, 6-H) = 7.9 Hz, 1H; 5-H), 7.14 (br ddd, ^{3}J (7-H, 8-H) = 8.3 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.9 Hz, 1H; 7-H), 7.30−7.38 (m, 1H; 17-H), 7.38−7.42 ppm (m, 4H; 15-H, 16-H, 18-H and 19-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.4 (C-11), 24.8 (C-4), 66.0 (C-13), 100.6 (C-3), 116.0 (C-8), 120.5 (C-10), 124.2 (C-6), 127.5 (C-7), 128.0 (C-15, 19), 128.1 (C-17), 128.6 (C-16, 18), 128.8 (C-5), 136.4 (C-14), 150.1 (C-9), 161.3 (C-2), 167.4 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 281 (16) $[M+1]^+$, 280 (47) $[M^+]$, 279 (80) $[M-1]^+$, 278 (15) $[M-2]^+$, 261 (5), 189 (100) $[M-C_7H_7]^+$, 173 (96) $[C_{11}H_9O_2]^+$, 144 (68) $[C_{10}H_8O]^+$, 131 (9) $[C_9H_7O]^+$, 115 (32) $[C_9H_7]^+$, 91 (85) $[C_7H_7]^+$, 77 (14) $[C_6H_5]^+$, 65 (7) $[C_5H_5]^+$; **HRMS** (EI, M^+) calcd for $C_{18}H_{16}O_3$: 280.1100; found: 280.1091.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-*tert*-butyl ester (3d)



3d

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 316 mg (2.0 mmol) *tert*-butyl acetoacetate (**2d**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 186 mg (76%) 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-*tert*-butyl ester (**3d**) as a pale yellow oil.



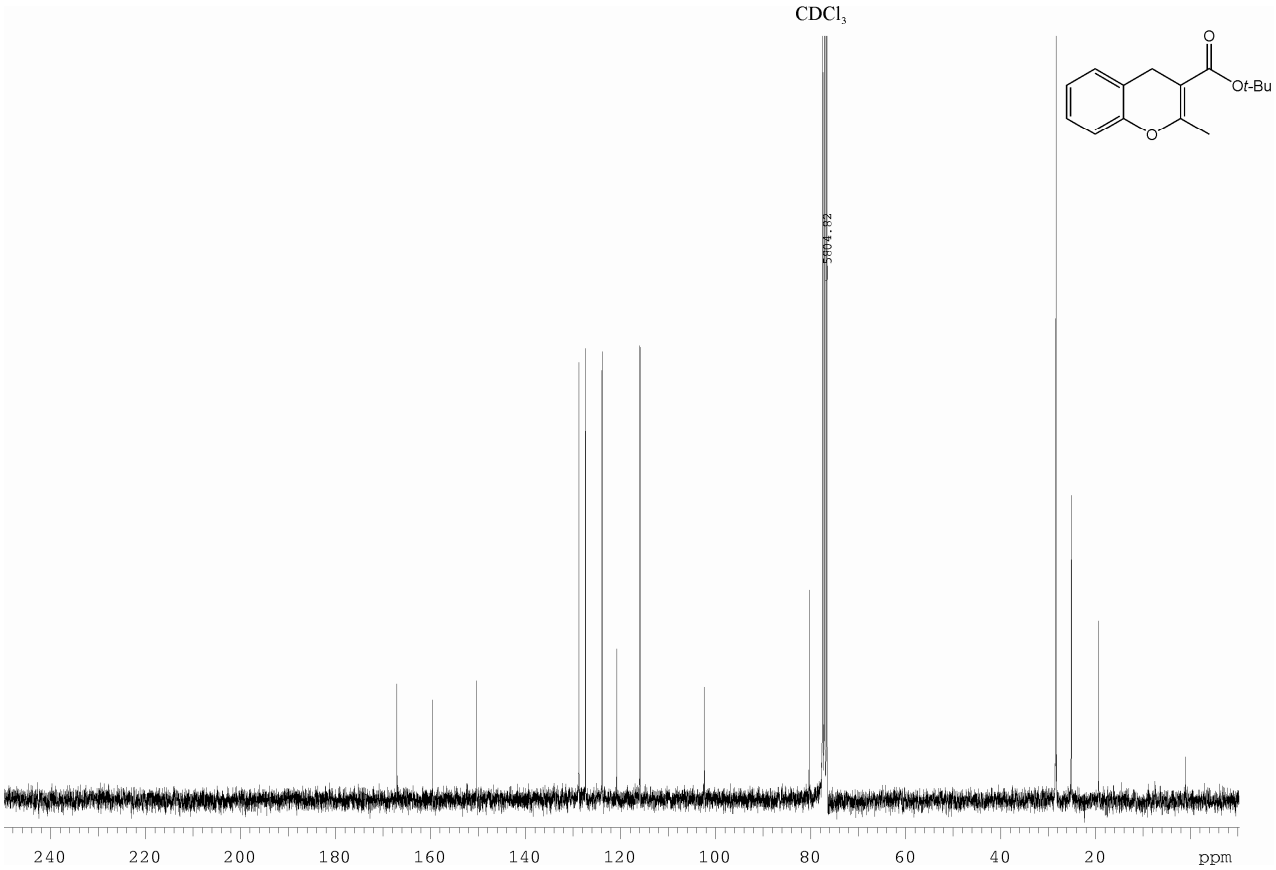
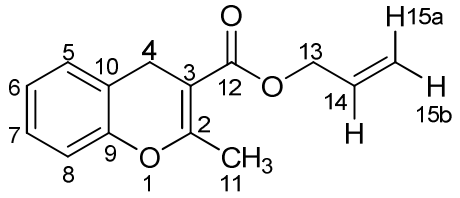


Figure 2. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3d** in $CDCl_3$.

$\boldsymbol{R_f}$ = 0.79 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2976 (m; CH_2, CH_3), 1708 (s; C=O), 1687 (s; C=O), 1647 (s; alkene C=C), 1587 (m; arom. C=C), 1491 (m; arom. C=C), 1458 (s; alkane C-H), 1381 (m; alkane C-H), 1365 (s), 1293 (m; ester C-O), 1251 (s; ether C-O), 1229 (s), 1161 (s), 1104 (s), 1059 (s), 1033 (s), 982 (s), 930 (w), 872 (m; arom. C-H), 839 (s), 750 (s; alkane C-H), 705 cm^{-1} (w); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 211 (4.08), 231 (4.03), 279 (3.99), 328 nm (3.59); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.52 (s, 9H; 14a-H_3, 14b-H_3 and 14c-H_3), 2.34 (s, 3H; 11-H_3), 3.55 (s, 2H; 4-H_2), 6.88 (dd, ^{3}J (7-H, 8-H) = 8.2 Hz, ^{4}J (6-H, 8-H) = 1.5 Hz, 1H; 8-H), 7.00 (ddd, ^{3}J (5-H, 6-H) = 7.7 Hz, ^{3}J (6-H, 7-H) = 7.0 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.09 (br d, ^{3}J (5-H, 6-H) = 8.1 Hz, 1H; 5-H), 7.12 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.0 Hz, ^{3}J (6-H, 7-H) = 7.2 Hz, ^{4}J (5-H, 7-H) = 1.9 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.3 (C-11), 25.1 (C-4), 28.5 (C-14a, 14b, 14c), 80.3 (C-13), 102.4 (C-3), 115.9 (C-8), 120.8 (C-10), 123.9 (C-6), 127.4 (C-7), 128.7 (C-5), 150.3 (C-9), 159.5 (C-2), 167.1 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 247 (4) $[M+1]^+$, 246 (32) $[M^+]$, 245 (87) $[M-1]^+$, 244 (9) $[M-2]^+$, 205 (47), 189 (100) $[M-C_4H_9]^+$, 173 (84) $[C_{11}H_9O_2]^+$, 144 (72) $[C_{10}H_8O]^+$, 115 (58) $[C_9H_7]^+$, 89 (53) $[C_7H_5]^+$, 86 (10), 63 (20) $[C_5H_3]^+$, 57 (67); **HRMS** (EI, M^+) calculated for $C_{15}H_{18}O_3$: 246.1256; found: 246.1234; **Elemental analysis** (%) calcd for $C_{15}H_{18}O_3$ (246.1256): C 73.15, H 7.37; found: C 72.89, H 7.34.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-allyl ester (3e)



3e

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 284 mg (2.0 mmol) allyl acetoacetate (**2e**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 149 mg (65%) 4*H*-1-benzopyran-3-carboxylic acid-2-methyl-allyl ester (**3e**) as a pale yellow oil.

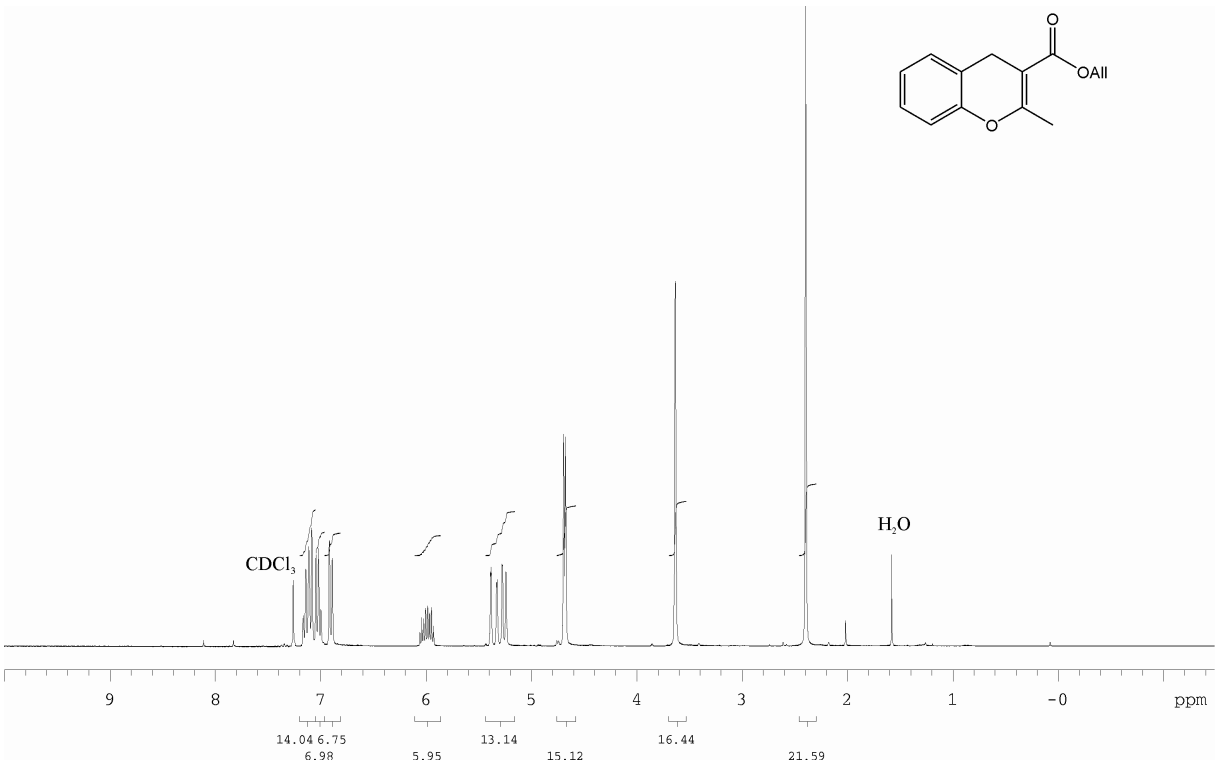
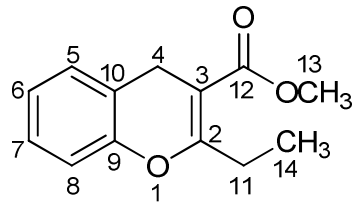


Figure 3. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3e** in $CDCl_3$.

$\boldsymbol{R_f}$ = 0.64 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2970 (w; CH_2, CH_3), 1713 (s; C=O), 1645 (s; alkene C=C), 1586 (m; arom. C=C), 1491 (m; arom. C=C), 1459 (m; alkane C-H), 1381 (m; alkane C-H), 1287 (m; ester C-O), 1237 (s; ether C-O), 1218 (s), 1185 (s), 1138 (m), 1103 (s), 1054 (s), 985 (s), 929 (s), 870 (m; arom. C-H), 827 (m), 751 (s; alkane C-H), 697 cm^{-1} (w); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 211 (4.07), 281 (3.92), 330 nm (3.42); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.40 (t, ^{2}J (11-H, 11-H) = 1.3 Hz, 3H; 11-H_3), 3.63 (br s, 2H; 4-H_2,), 4.68 (dt, ^{3}J (13-H, 14-H) = 5.5 Hz, ^{2}J (13-H, 13-H) = 1.5 Hz, 2H; 13-H_2), 5.26 (dq, $^{3}J_{cis}$ (14-H, 15b-H) = 10.3 Hz, ^{2}J (15a-H, 15b-H) = 1.3 Hz, 1H; 15b-H), 5.35 (dq, $^{3}J_{trans}$ (14-H, 15a-H) = 17.2 Hz, ^{2}J (15a-H, 15b-H) = 1.6 Hz, 1H; 15a-H), 5.99 (ddt, ^{3}J (13-H, 14-H) = 5.5 Hz, $^{3}J_{cis}$ (14-H, 15b-H) = 10.3 Hz, $^{3}J_{trans}$ (14-H, 15a-H) = 17.1 Hz, 1H; 14-H), 6.90 (dd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{4}J (6-H, 8-H) = 1.4 Hz, 1H; 8-H), 7.02 (ddd, ^{3}J (5-H, 6-H) = 7.7 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.10 (br d, ^{3}J (5-H, 6-H) = 8.0 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.9 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.3 (C-11), 24.8 (C-4), 64.8 (C-13), 100.7 (C-3), 116.0 (C-8), 117.8 (C-15), 120.4 (C-10), 124.1 (C-6), 127.5 (C-7), 128.8 (C-5), 132.6 (C-14), 150.1 (C-9), 161.1 (C-2), 167.2 ppm (C-12); **MS** (GC-MS): *m/z* (%) = 231 (6) $[M+1]^+$, 230 (3) $[M^+]$, 229 (12) $[M-1]^+$, 189 (100) $[M-C_3H_5]^+$, 171 (47) [189–H_2O], 145 (23) $[C_{10}H_9O]^+$, 115 (52) $[C_9H_7]^+$, 91(8) $[C_7H_7]^+$, 63 (8) $[C_5H_3]^+$; **HRMS** (EI, M^+) calculated for $C_{14}H_{14}O_3$: 230.0942; found: 230.0954.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-ethyl-methyl ester (3f)[1]

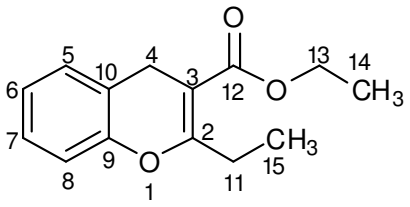


3f

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 260 mg (2.0 mmol) methyl propionylacetate (**2f**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 180 mg (83%) 4*H*-1-benzopyran-3-carboxylic acid-2-ethyl-methyl ester (**3f**) as a pale yellow oil.

$\boldsymbol{R_f}$ = 0.72 (cyclohexane/EtOAc = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.20 (t, ^3J (11-H, 14-H) = 7.5 Hz, 3H; 14-H_3), 2.81 (q, ^3J (11-H, 14-H) = 7.5 Hz, 2H; 11-H_2), 3.61 (s, 2H; 4-H_2), 3.77 (s, 3H; 13-H_3), 6.92 (dd, ^3J (7-H, 8-H) = 8.1 Hz, 1H; 8-H), 7.00-7.18 ppm (m, 3H; 5-H, 6-H and 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 11.7 (C-14), 24.9 (C-11), 25.7 (C-4), 51.4 (C-13), 100.0 (C-3), 116.0 (C-8), 120.5 (C-10), 124.0 (C-6), 127.5 (C-7), 128.7 (C-5), 150.3 (C-9), 165.6 (C-2), 167.8 ppm (C-12); **MS** (GC-MS): *m/z* (%) = 218 (17) [M^+], 203 (100) [M–CH_3]$^+$, 185 (18) [203–H_2O], 159 (25) [$C_{11}H_{11}O$]$^+$, 144 (15) [$C_{10}H_8O$]$^+$, 128 (9) [$C_{10}H_8$]$^+$, 115 (22) [C_9H_7]$^+$, 102 (6) [C_8H_6]$^+$, 91 (7) [C_7H_7]$^+$, 77 (8) [C_6H_5]$^+$.

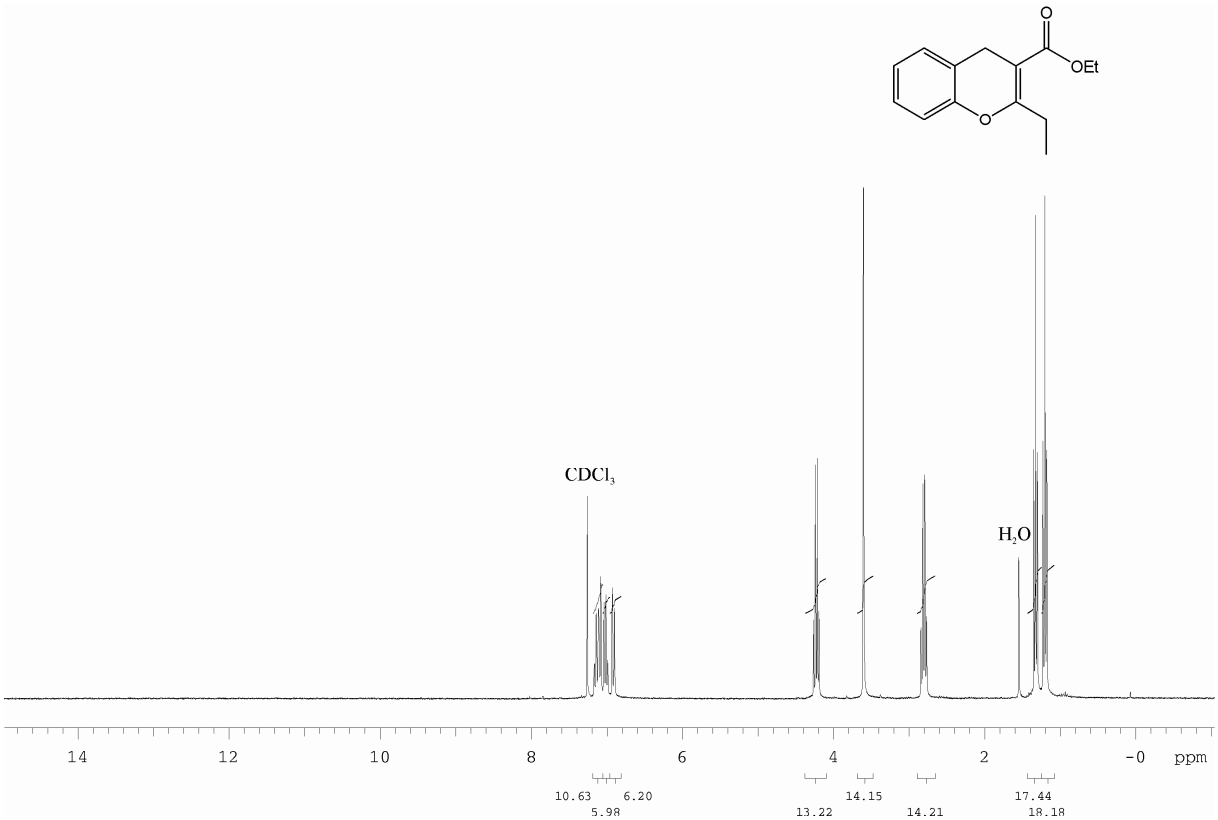
Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-ethyl-ethyl ester (3g)



3g

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 288 mg (2.0 mmol) ethyl propionylacetate (**2g**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h.

Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 204 mg (88%) 4*H*-1-benzopyran-3-carboxylic acid-2-ethyl-ethyl ester (**3g**) as a colourless solid.



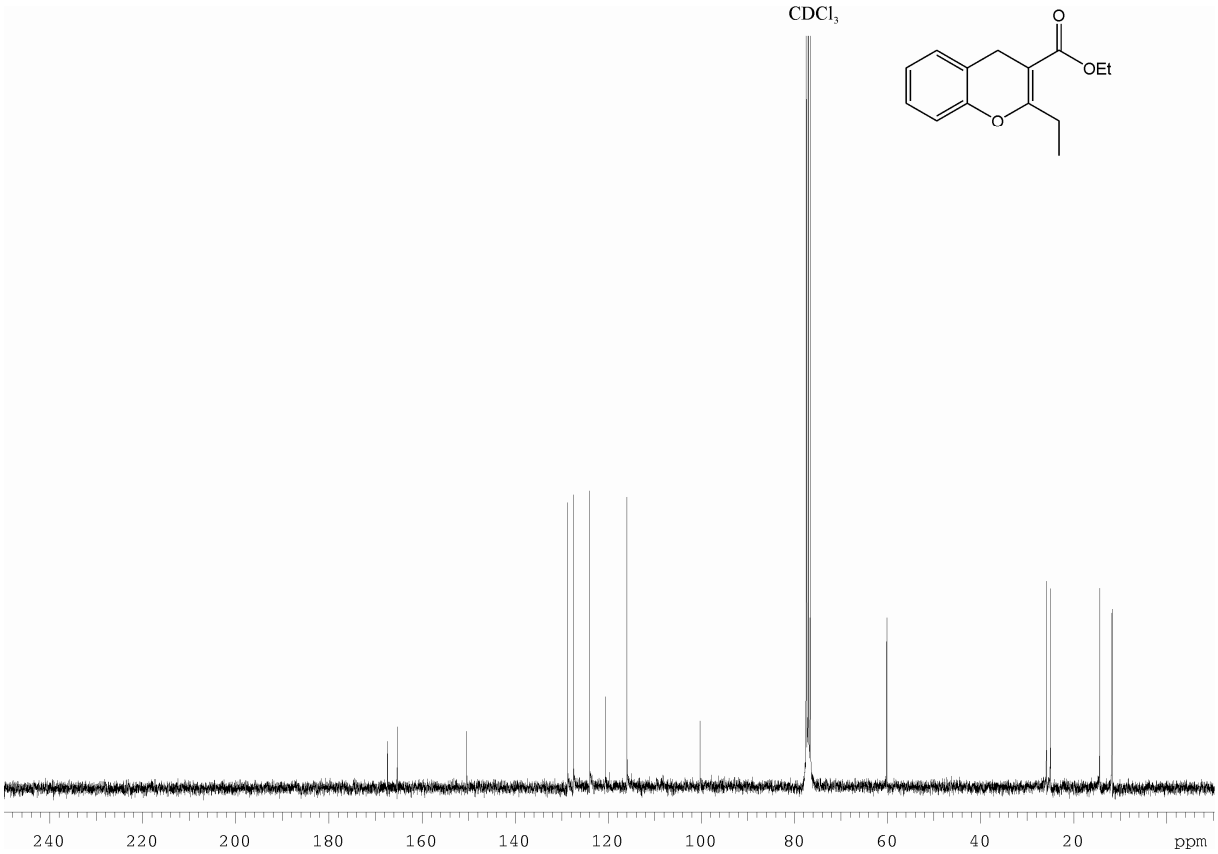
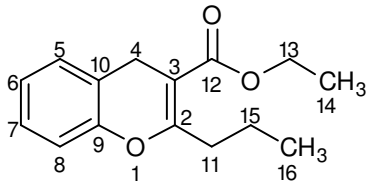


Figure 4. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3g** in $CDCl_3$.

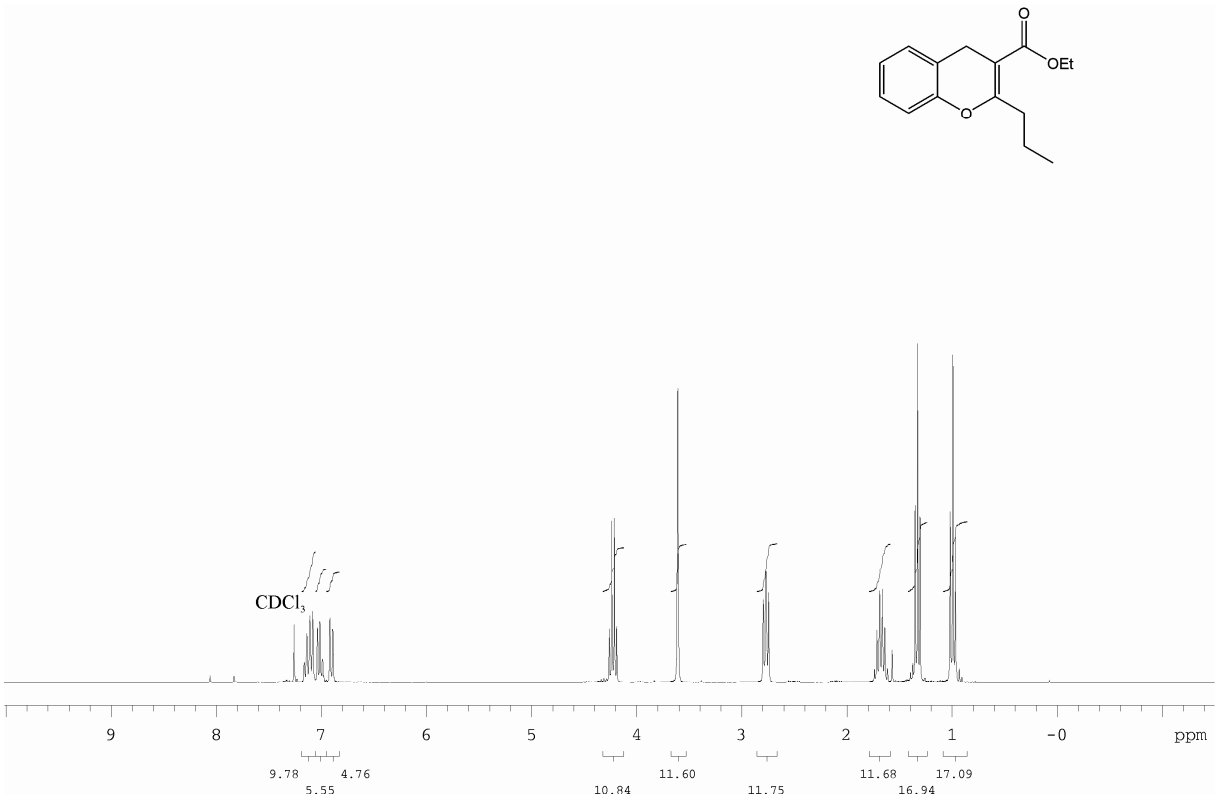
M.p. 45-47 °C; $\boldsymbol{R_f}$ = 0.88 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2990 (m; CH_2, CH_3), 2920 (m; CH_2, CH_3), 1750 (s; C=O), 1712 (s; C=O), 1660 (s; alkene C=C), 1500 (s; arom. C=C), 1459 (m; alkane C-H), 1360 (m; alkane C-H), 1286 (s; ester C-O), 1221 (s; ether C-O), 1185 (s), 1111 (s), 1095 (s), 1040 (s), 960 (s), 940 (s), 861 (s; arom. C-H), 813 (s), 769 (m), 751 (m; alkane C-H), 705 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 276 nm (3.81); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.21 (t, ^{3}J (11-H, 15-H) = 7.5 Hz, 3H; 15-H_3), 1.33 (t, ^{3}J (13-H, 14-H) = 7.2 Hz, 3H; 14-H_3), 2.81 (q, ^{3}J (11-H, 15-H) = 7.5 Hz, 2H; 11-H_2), 3.60 (s, 2H; 4-H_2), 4.23 (q, ^{3}J (13-H, 14-H) = 7.2 Hz, 2H; 13-H_2), 6.92 (dd, ^{3}J (7-H, 8-H) = 8.2 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 8-H), 7.02 (ddd, ^{3}J (5-H, 6-H) = 7.3 Hz, ^{3}J (6-H, 7-H) = 7.3 Hz, ^{4}J (6-H, 8-H) = 1.2 Hz, 1H; 6-H), 7.09 (br d, ^{3}J (5-H, 6-H) = 7.5 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.0 Hz, ^{3}J (6-H, 7-H) = 7.3 Hz, ^{4}J (5-H, 7-H) = 1.7 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 11.8 (C-15), 14.3 (C-14), 24.9 (C-4), 25.8 (C-11), 60.1 (C-13), 100.3 (C-3), 116.0 (C-8), 120.6 (C-10), 124.0 (C-6), 127.5 (C-7), 128.7 (C-5), 150.4 (C-9), 165.3 (C-2), 167.4 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 233 (18) $[M+1]^+$, 232 (84) $[M^+]$, 231 (48) $[M-1]^+$, 203 (100) $[M-Et]^+$, 187 (88) $[C_{12}H_{11}O_2]^+$, 185 (78), 157 (82) $[C_{11}H_9O]^+$, 144 (69) $[C_{10}H_8O]^+$, 131 (40) $[C_9H_7O]^+$, 115 (73) $[C_9H_7]^+$, 91 (24) $[C_7H_7]^+$, 77 (17) $[C_6H_5]^+$, 63 (8) $[C_5H_3]^+$; **HRMS** (EI, M^+) calculated for $C_{14}H_{16}O_3$: 232.1100; found: 232.1122; **Elemental analysis (%)** calculated for $C_{14}H_{16}O_3$ (232.1100): C 72.39, H 6.94; found: C 72.33, H 6.90.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-*n*-propyl-ethyl ester (3h)



3h

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 316 mg (2.0 mmol) ethyl butyrylacetate (**2h**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 209 mg (85%) 4*H*-1-benzopyran-3-carboxylic acid-2-*n*-propyl-ethyl ester (**3h**) as a pale yellow oil.



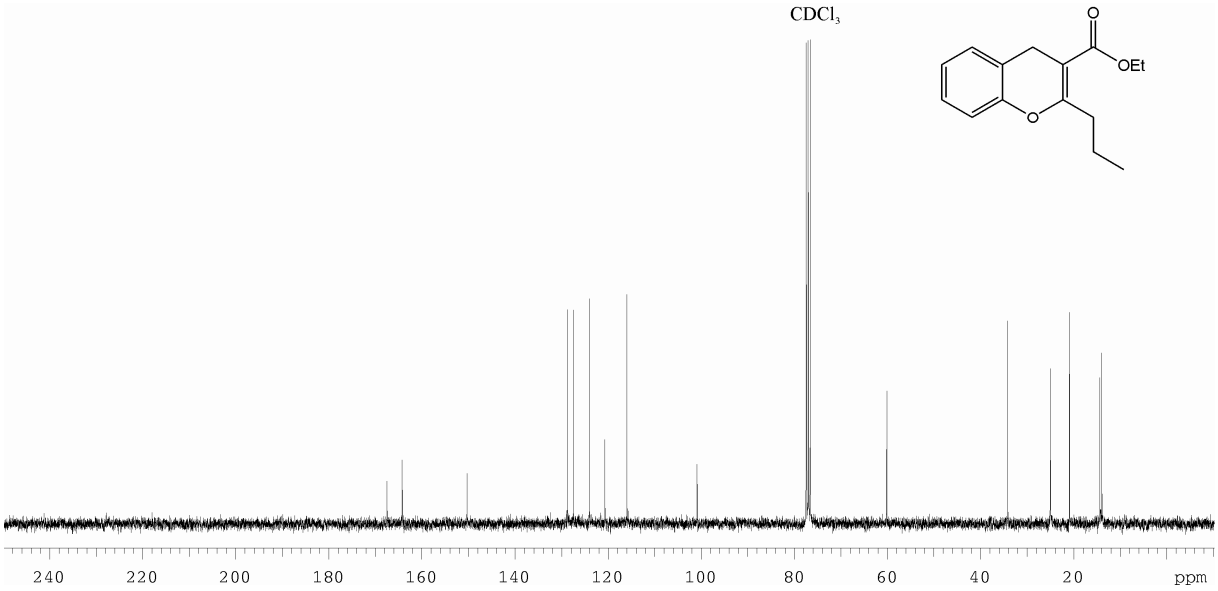
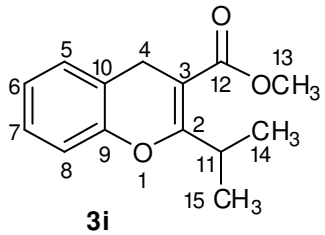


Figure 5. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3h** in $CDCl_3$.

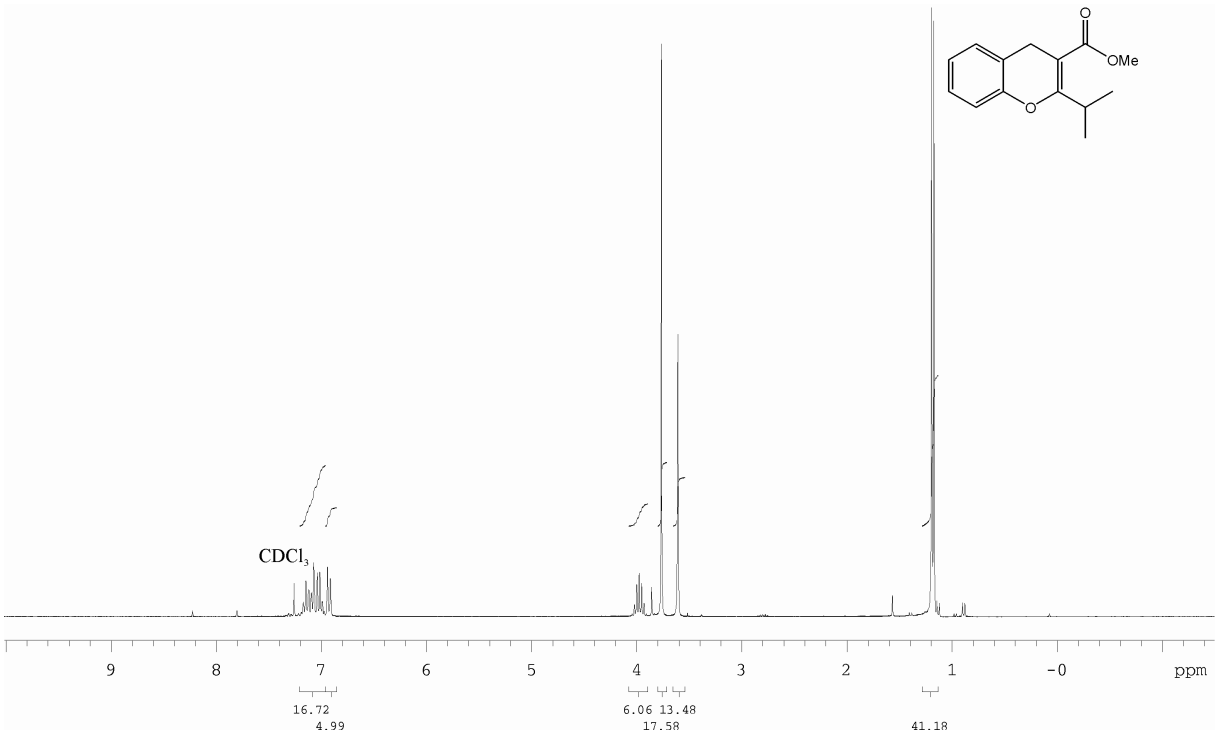
R_f = 0.83 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2962 (m; CH_2, CH_3), 1712 (s; C=O), 1642 (s; alkene C=C), 1585 (m; arom. C=C), 1491 (m; arom. C=C), 1458 (m; alkane C-H), 1369 (m; alkane C-H), 1285 (m; ester C-O), 1218 (s; ether C-O), 1186 (s), 1134 (m), 1104 (s), 1082 (m), 1043 (s), 949 (m), 901 (m), 858 (m; arom. C-H), 751 cm^{-1} (s; alkane C-H); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 212 (4.06), 232 (4.05), 280 (3.99), 331 nm (3.61); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.99 (t, ^{3}J (15-H, 16-H) = 7.4 Hz, 3H; 16-H_3), 1.33 (t, ^{3}J (13-H, 14-H) = 7.1 Hz, 3H; 14-H_3), 1.61-1.75 (m, 2H; 15-H_2), 2.74-2.80 (m, 2H; 11-H_2), 3.61 (s, 2H; 4-H_2), 4.23 (q, ^{3}J (13-H, 14-H) = 7.2 Hz, 2H; 13-H_2), 6.91 (dd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{4}J (6-H, 8-H) = 1.5 Hz, 1H; 8-H), 7.01 (ddd, ^{3}J (5-H, 6-H) = 7.4 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.10 (dt, ^{3}J (5-H, 6-H) = 7.7 Hz, ^{4}J (5-H, 7-H) = 2.1 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.9 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 13.9 (C-16), 14.3 (C-14), 20.9 (C-15), 24.9 (C-4), 34.7 (C-11), 60.2 (C-13), 101.9 (C-3), 115.9 (C-8), 120.7 (C-10), 124.0 (C-6), 127.4 (C-7), 128.7 (C-5), 150.3 (C-9), 164.2 (C-2), 167.5 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 247 (16) $[M+1]^+$, 246 (80) $[M^+]$, 245 (66) $[M-1]^+$, 244 (12) $[M-2]^+$, 217 (100) $[M-Et]^+$, 201 (86) $[C_{13}H_{13}O_2]^+$, 173 (93) $[C_{12}H_{13}O]^+$, 157 (34) $[C_{11}H_9O]^+$, 144 (78) $[C_{10}H_8O]^+$, 115 (57) $[C_9H_7]^+$, 77 (14) $[C_6H_5]^+$; **HRMS** (EI, M^+) calculated for $C_{15}H_{18}O_3$: 246.1256; found: 246.1224.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-*iso*-propyl-methyl ester (3i)



3i

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 288 mg (2.0 mmol) methyl 4-methyl-3-oxovalerate (**2i**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 197 mg (85%) 4*H*-1-benzopyran-3-carboxylic acid-2-*iso*-propyl-methyl ester (**3i**) as a pale yellow oil.



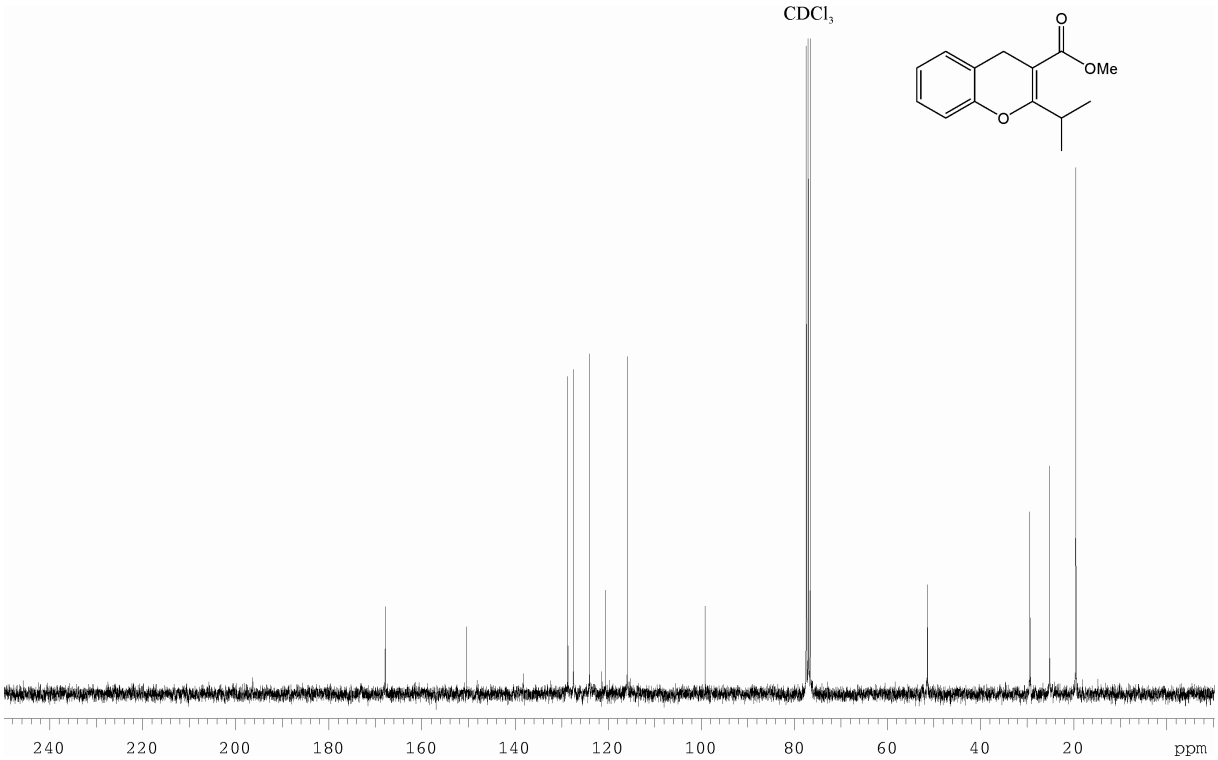
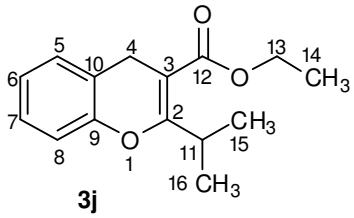


Figure 6. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3i** in $CDCl_3$.

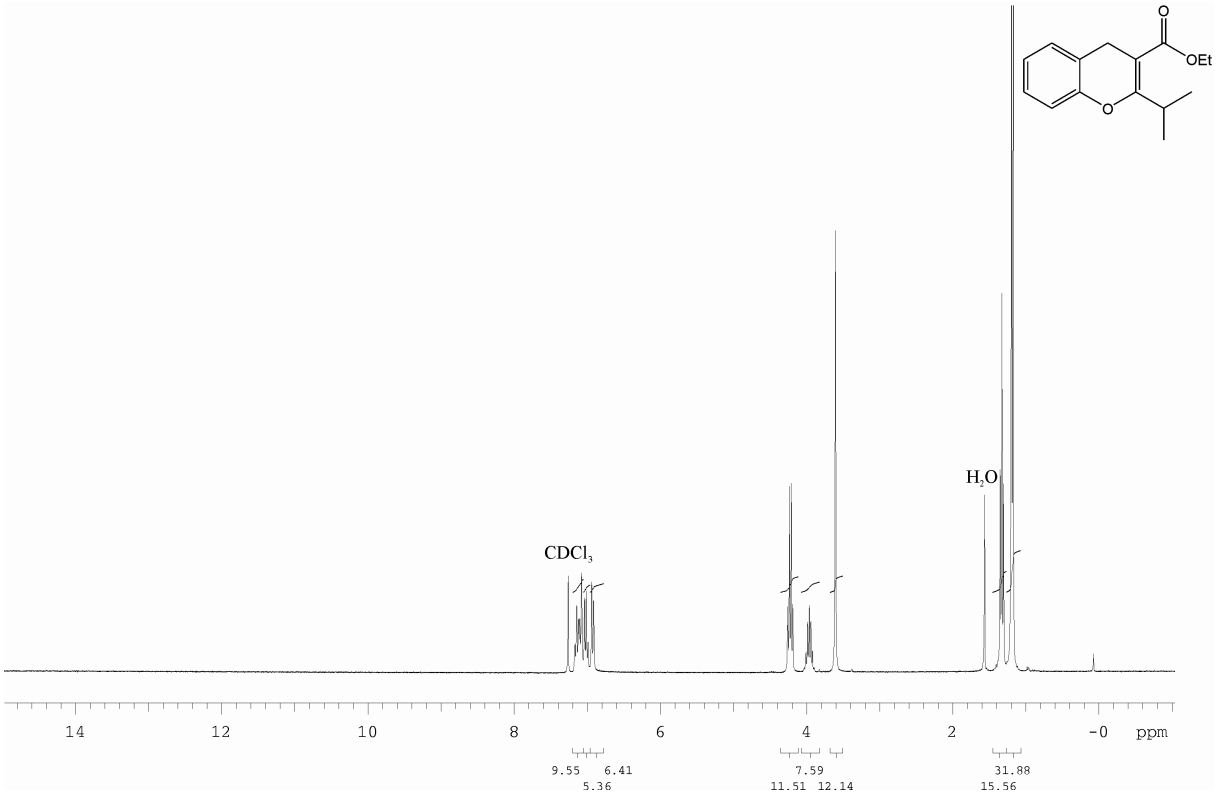
$\boldsymbol{R_f}$ = 0.65 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2968 (m; CH_2, CH_3), 1712 (s; C=O), 1637 (s; alkene C=C), 1586 (m; arom. C=C), 1491 (m; arom. C=C), 1459 (m; alkane C-H), 1434 (m), 1360 (m; alkane C-H), 1286 (m; ester C-O), 1259 (m), 1238 (m; ether C-O), 1220 (s), 1185 (s), 1111 (m), 1094 (m), 1062 (s), 1039 (s), 972 (m), 940 (m), 885 (m), 861 (m; arom. C-H), 813 (m), 769 (s), 751 (s; alkane C-H), 705 cm^{-1} (w); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 213 (3.92), 232 (3.91), 280 (3.81), 332 nm (3.40); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.18 (d, ^{3}J (11-H, 14-H or 15-H) = 6.8 Hz, 6H; 14-H_3, and 15-H_3), 3.61 (br s, 2H; 4-H_2), 3.76 (s, 3H; 13-H_3), 3.97 (sept, ^{3}J (11-H, 14-H or 15-H) = 6.8 Hz, 1H; 11-H), 6.90 (dd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{4}J (6-H, 8-H) = 1.4 Hz, 1H; 8-H), 7.01 (ddd, ^{3}J (5-H, 6-H) = 7.5 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.08 (br d, ^{3}J (5-H, 6-H) = 8.0 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 2.0 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.5 (C-14, 15), 25.2 (C-4), 29.4 (C-11), 50.5 (C-13), 99.1 (C-3), 115.9 (C-8), 120.6 (C-10), 124.0 (C-6), 127.5 (C-7), 128.7 (C-5), 150.4 (C-9), 167.8 (C-2), 167.9 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 233 (18) $[M+1]^+$, 232 (80) $[M^+]$, 231 (97) $[M-1]^+$, 217 (80) $[M-CH_3]^+$, 204 (67), 199 (42), 173 (100) $[C_{12}H_{13}O]^+$, 157 (38) $[C_{11}H_9O]^+$, 146 (44) $[C_{10}H_{10}O]^+$, 128 (19) [146–H_2O], 115 (14) $[C_9H_7]^+$, 101 (44) $[C_8H_5]^+$, 89 (24) $[C_7H_5]^+$, 63 (6) $[C_5H_3]^+$; **HRMS** (EI, M^+) calculated for $C_{14}H_{16}O_3$: 232.1099; found: 232.1092.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-*iso*-propyl-ethyl ester (3j)



3j

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 316 mg (2.0 mmol) ethyl isobutyrylacetate (**2j**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 196 mg (80%) 4*H*-1-benzopyran-3-carboxylic acid-2-*iso*-propyl-ethyl ester (**3j**) as a colourless solid.



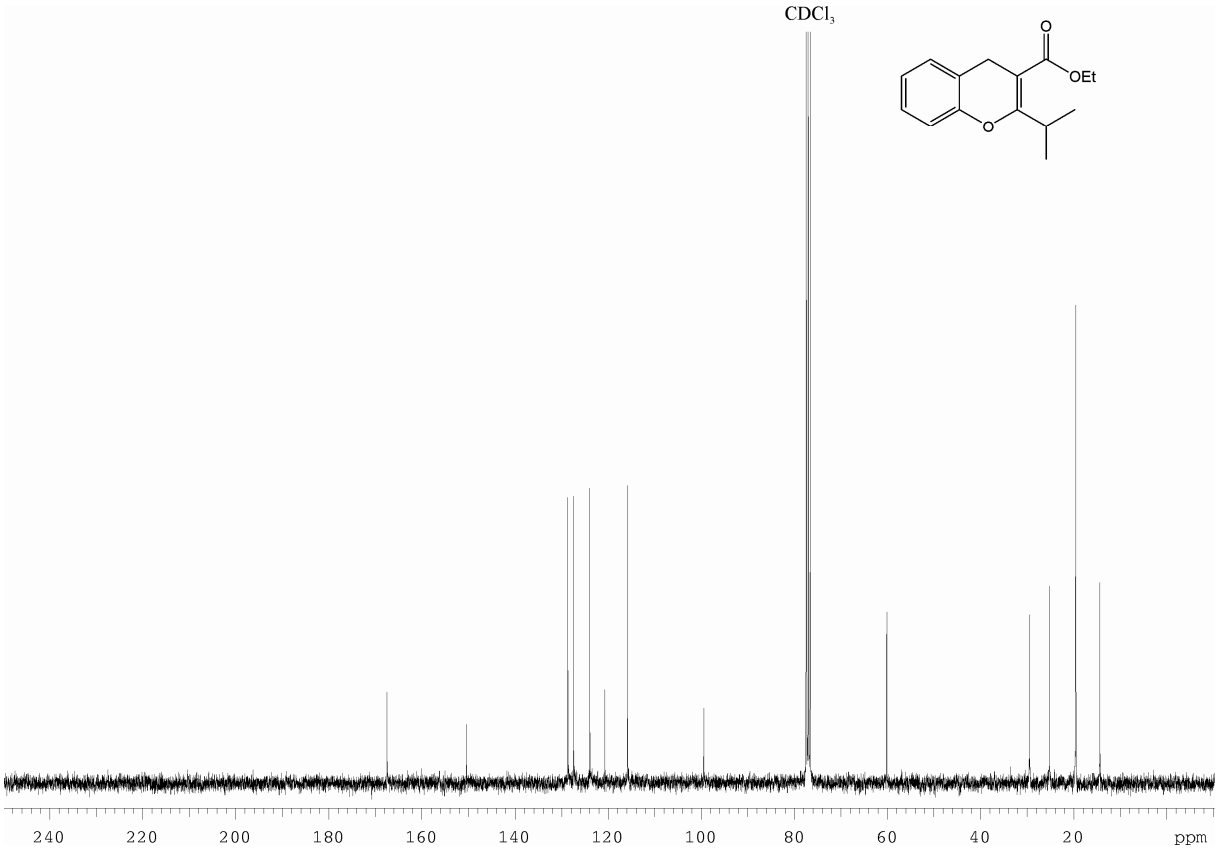
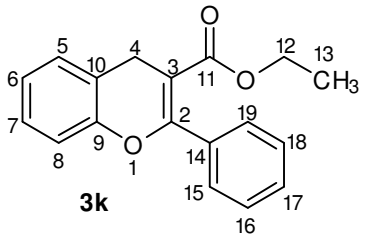


Figure 7. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **3j** in $CDCl_3$.

M.**p**. 42-44 °C; $\boldsymbol{R_f}$ = 0.8 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2990 (m; CH_2, CH_3), 2930 (m; CH_2, CH_3), 1720 (s; C=O), 1660 (s; alkene C=C), 1585 (s; arom. C=C), 1515 (s; arom. C=C), 1490 (s; arom. C=C), 1370 (m; alkane C-H), 1295 (s; ester C-O), 1260 (s; ether C-O), 1248 (s; ether C-O), 1225 (s), 1201 (s), 1111 (s), 1098 (s), 1061 (s), 1044 (s), 1030 (s), 971 (s), 925 (s), 884 (s; arom. C-H), 860 (s; arom. C-H), 820 (s), 769 (m), 751 (m; alkane C-H), 705 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 276 nm (3.82); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.18 (d, ^{3}J (15-H, 16-H) = 6.8 Hz, 6H; 15-H_3 and 16-H_3), 1.33 (t, ^{3}J (13-H, 14-H) = 7.1 Hz, 3H; 14-H_3), 3.61 (s, 2H; 4-H_3), 3.96 (sept, ^{3}J (11-H, 15-H) = 6.9 Hz, 1H; 11-H), 4.22 (q, ^{3}J (13-H, 14-H) = 6.9 Hz, 2H; 13-H_2), 6.90 (dd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 8-H), 7.01 (ddd, ^{3}J (5-H, 6-H) = 7.5 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (6-H, 8-H) = 1.2 Hz, 1H; 6-H), 7.09 (br d, ^{3}J (5-H, 6-H) = 7.9 Hz, 1H; 5-H), 7.14 ppm (br ddd, ^{3}J (7-H, 8-H) = 8.1 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.8 Hz, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.3 (C-14), 19.5 (C-15, 16), 25.3 (C-4), 29.4 (C-11), 60.1 (C-13), 99.4 (C-3), 115.9 (C-8), 120.7 (C-10), 123.9 (C-6), 127.4 (C-7), 128.6 (C-5), 150.4 (C-9), 167.48 (C-2), 167.52 ppm (C-12); **MS** (EI, 70 eV): *m/z* (%) = 246 (11) [M^+], 245 (73) [M–1]$^+$, 244 (7) [M–2]$^+$, 216 (67) [M–Et]$^+$, 199 (12), 173 (100) [$C_{12}H_{13}O$]$^+$, 146 (78) [$C_{10}H_{10}O$]$^+$, 118 (17) [$C_{10}H_{10}O$–CO]$^+$, 101 (28) [C_8H_5]$^+$, 89 (36) [C_7H_5]$^+$, 63 (15) [C_5H_3]$^+$; **HRMS** (EI,

M^+) calculated for $C_{15}H_{18}O_3$: 246.1256; found: 246.1255; **Elemental analysis (%)** calculated for $C_{15}H_{18}O_3$ (246.1256): C 73.15, H 7.37; found: C 72.95, H 7.29.

Synthesis of 4*H*-1-benzopyran-3-carboxylic acid-2-phenyl-ethyl ester (3k)[1]

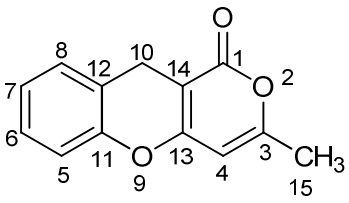


3k

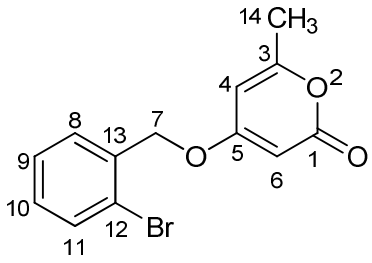
According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 384 mg (2.0 mmol) ethyl benzoylacetate (**2k**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 226 mg (81%) 4*H*-1-benzopyran-3-carboxylic acid-2-phenyl-ethyl ester (**3k**) as a colourless solid.

M.**p**. 42-44 °C; $\boldsymbol{R_f}$ = 0.53 (cyclohexane/EtOAc = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 0.97 (t, ^3J (12-H, 13-H) = 7.2 Hz, 3H; 13-H_3), 3.79 (s, 2H; 4-H_2), 4.00 (q, ^3J (12-H, 13-H) = 7.2 Hz, 2H; 12-H_2), 6.97 (d, ^3J (7-H, 8-H) = 7.8 Hz, 1H; 8-H), 7.07 (t, ^3J (6-H, 5-H and 7-H) = 6.3 Hz, 1H; 6-H), 7.17 (m, 2H; 5-H and 7-H), 7.39-7.46 ppm (m, 5H; 15-H,16-H,17-H,18-H and 19-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 13.6 (C-13), 25.7 (C-4), 60.1 (C-12), 102.8 (C-3), 116.3 (C-8), 120.2 (C-10), 124.3 (C-6), 127.6 (C-7), 127.8 (C-5), 128.5 (C-15), 128.8 (19), 129.3 (C-16), 130.4 (C-18), 132.8 (C-17), 135.5 (C-14), 150.7 (C-9), 159.0 (C-2), 167.5 ppm (C-11); **MS** (GC-MS): *m/z* (%) = 280 (10) [M^+], 251 (100) [M–Et]$^+$, 235 (9) $[C_{16}H_{11}O_2]^+$, 207 (31) $[C_{15}H_{11}O]^+$, 178 (27), 152 (9), 129 (10), 105 (11), 77 (11) $[C_6H_5]^+$.

Synthesis of 3-methyl 10*H*-pyrano[4,3-*b*]chromen-1-one (5)

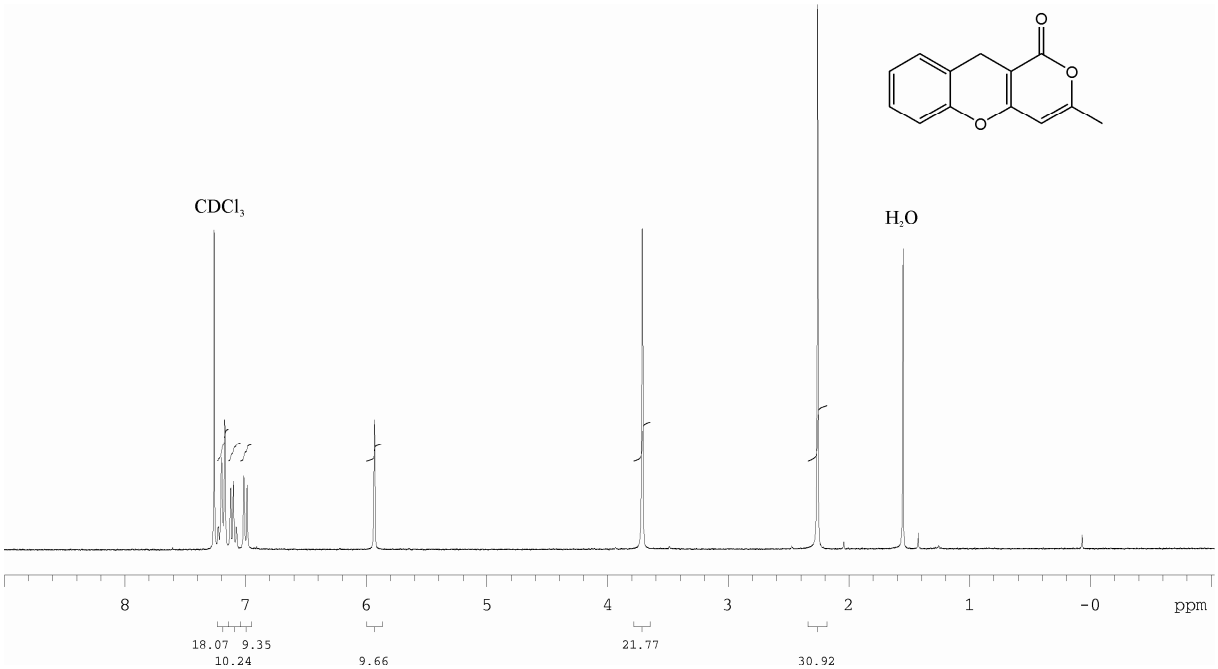


5



6

According to the general procedure I, 249 mg (1.0 mmol) 2-bromobenzyl bromide (**1a**), 252 mg (2.0 mmol) 4-hydroxy-6-methyl-pyrone (**4**), 39 mg (0.2 mmol) CuI (98%) and 875 mg (4.0 mmol) K_3PO_4 (97%) were reacted in 3 mL *N*,*N*-dimethyl formamide in a sealed vial in an argon atmosphere at 110 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 70:2) afforded 95 mg (45%) 3-methyl 10*H*-pyrano[4,3-*b*]chromen-1-one (**5**) as a pale yellow solid and 57 mg (19%) 4-[(2-bromobenzyl)oxy]-6-methyl-2*H*-pyran-2-one (**6**) as a pale yellow solid.



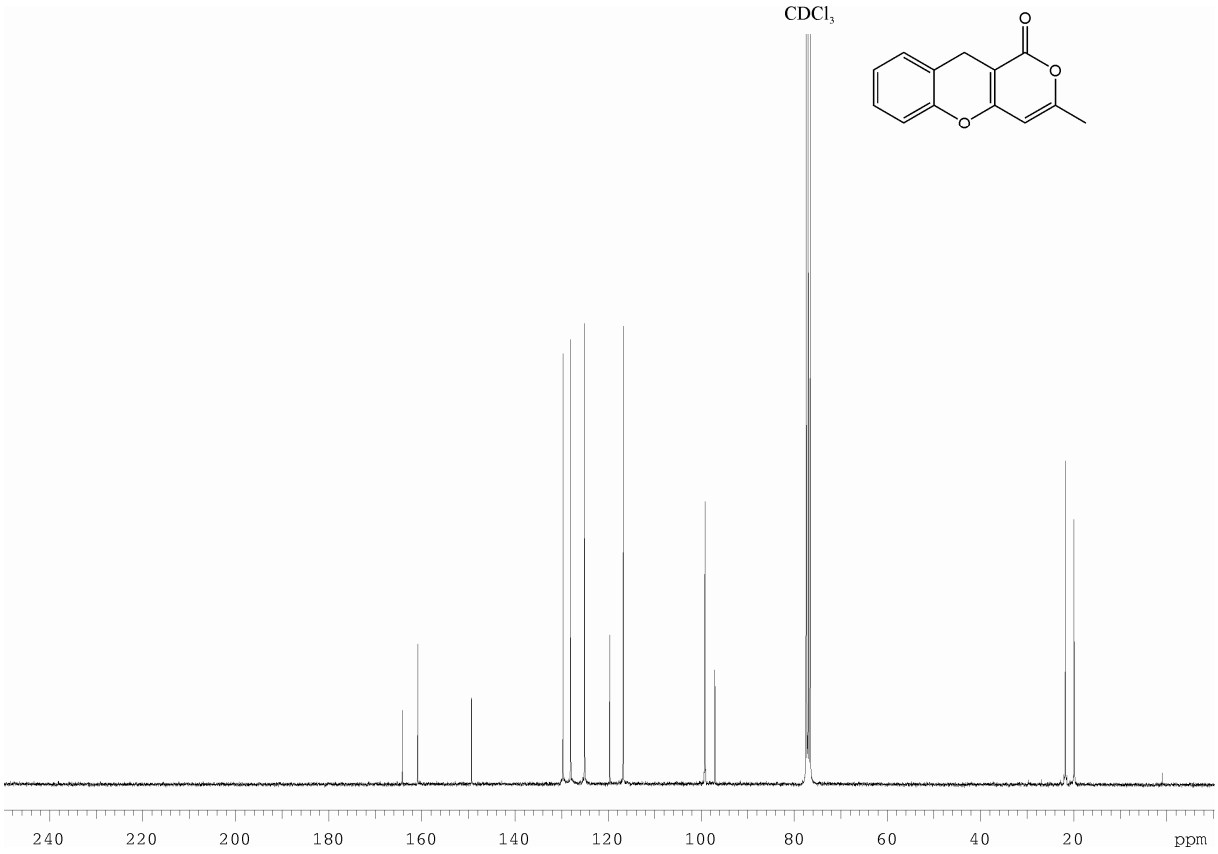
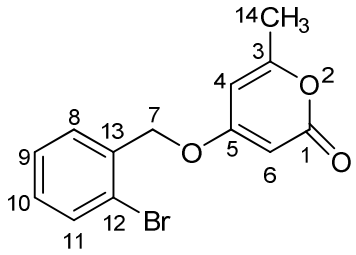


Figure 8. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **5** in $CDCl_3$.

M.**p**. 185-186 °C; $\boldsymbol{R_f}$ = 0.25 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3100 (w; CH_2, CH_3), 1690 (s; C=O), 1650 (m; alkene C=C), 1630 (m), 1600 (m), 1575 (m; arom. C=C), 1500 (m; arom. C=C), 1455 (m; alkane C-H), 1400 (m), 1390 (m; alkane C-H), 1365 (m), 1345 (m), 1310 (m), 1286 (m; ester C-O), 1240 (m; ether C-O), 1210 (m), 1185 (m), 1095 (m), 1010 (m), 970 (m), 890 (m; arom. C-H), 850 (m; arom. C-H), 751 (s; alkane C-H), 705 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 211 (4.40), 259 (3.96), 300 nm (3.54); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.26 (br d, ^{2}J (15-H, 15-H) = 0.9 Hz, 3H; 15-H_3), 3.71 (s, 2H; 10-H_2), 5.93 (br q, ^{4}J (4-H, 15-H) = 1.0 Hz, 1H; 4-H), 6.99 (dd, ^{3}J (5-H, 6-H) = 8.3 Hz, ^{4}J (5-H, 7-H) = 1.3 Hz, 1H; 5-H), 7.01 (ddd, ^{3}J (7-H, 8-H) = 7.7 Hz, ^{3}J (6-H, 7-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.3 Hz, 1H; 7-H), 7.18 (overlapped, 1H; 8-H), 7.19 ppm (overlapped, 1H; 6-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.8 (C-15), 21.7 (C-10), 97.0 (C-14), 99.2 (C-4), 116.7 (C-5), 119.6 (C-12), 125.0 (C-7), 128.0 (C-6), 129.7 (C-8), 149.3 (C-11), 160.86 (C-13), 160.90 (C-3), 164,2 ppm (C-1); **MS** (EI, 70 eV): *m/z* (%) = 215 (16) $[M+1]^+$, 214 (100) $[M^+]$, 213 (93) $[M-1]^+$, 185 (8), 171 (82), 115 (13) $[C_9H_7]^+$, 89 (4) $[C_7H_5]^+$, 63 (4) $[C_5H_3]^+$; **HRMS** (EI, M^+) calculated for $C_{13}H_{10}O_3$: 214.0630; found: 214.0620.

Characterization of 4-[(2-bromobenzyl)oxy]-6-methyl-2*H*-pyran-2-one (6)[2]

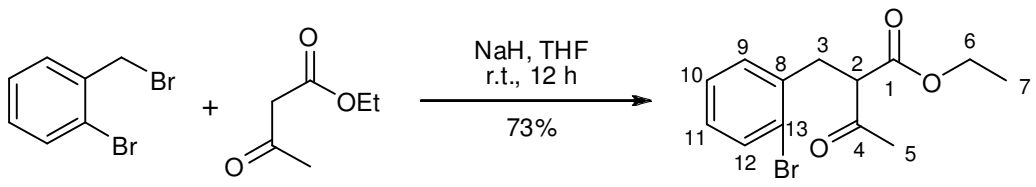


6

M.p.= 134-136 (ref [2] 135-135 °C); **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 2.17 (s, 3H; 14-H_3), 5.15 (s, 2H; 7-H_2), 5.69 (d, ^4J (4-H, 6-H) = 2.0 Hz, 1H; 6-H), 6.12 (s, 1H; 4-H), 7.36 (ddd, ^3J (9-H, 10-H) = 7.8 Hz, ^3J (8-H, 9-H) = 7.8 Hz, ^4J (9-H, 11-H) = 1.8 Hz, 1H; 9-H), 7.45 (ddd, ^3J (9-H, 10-H) = 7.8 Hz, ^3J (10-H, 11-H) = 8.0 Hz, ^4J (9-H, 11-H) = 1.8 Hz, 1H; 10-H), 7.57 (dd, ^3J (8-H, 9-H) = 7.5 Hz, ^4J (8-H, 10-H) = 1.5 Hz, 1H; 8-H), 7.70 (d, ^3J (10-H, 11-H) = 7.8 Hz, 1H; 11-H); **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 19.23 (C-14), 70.13 (C-7), 87.95 (C-6), 99.85 (C-4), 123.61 (C-12), 128.04 (C-10), 130.90 (C-9), 131.26 (C-8), 132.82 (C-11), 134.05 (C-13), 162.59 (C-3), 163.51 (C-5), 169.89 ppm (C-1).

5. Synthesis and characterization of starting materials 1c, 7, 10

Synthesis of ethyl 2-acetyl-3-(2-bromophenyl)propionate (7)[3]



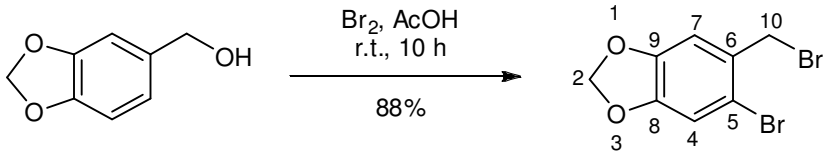
1a **2b** **7**

In an oven dried round-bottomed flask 1.30 g (10 mmol) of ethyl acetoacetate (**2b**) were dissolved in freshly dried 5 mL THF under argon atmosphere. The reaction mixture was cooled to 0 °C and 300 mg (10 mmol) NaH (80%) were added in several portions within 15 min. The reaction mixture was allowed to warm to room temperature and 1.25 g (5 mmol) of 2-bromobenzyl bromide (**1a**) were added dropwise. The reaction mixture was allowed to stirr at room temperature for 12 h. The reaction mixture was poured into 50 mL saturated NH_4Cl and extracted with EtOAc (3 × 50 mL). The combined organic layers were

dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. The residue thus obtained was purified by flash column chromatography over silica gel (cyclohexane/EtOAc = 20:1) and afforded 1.1 g (73%) of ethyl 2-acetyl-3-(2-bromophenyl)propionate (**7**) as a colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$): 1.2 (t, ^3J (6-H, 7-H) = 7.2 Hz, 3H; 7-H_3), 2.23 (s, 3H; 5-H_3), 3.27 (m, 2H; 3-H_2), 3.97 (t, ^3J (2-H, 3-H) = 6.9 Hz, 1H; 2-H), 4.12 (q, ^3J (6-H, 7-H) = 7.2 Hz, 2H; 6-H_2), 7.08 (ddd, ^3J (9-H, 10-H) = 7.5 Hz, ^3J (10-H, 11-H) = 7.2 Hz, ^4J (10-H, 12-H) = 1.8 Hz, 1H; 10-H), 7.18-7.24 (overlapped, 2H; 11-H and 12-H), 7.53 (d, ^3J (9-H, 10-H) = 8.1 Hz, 1H; 9-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 13.96 (C-7), 29.64 (C-5), 34.17 (C-2), 58.77 (C-6), 61.44 (C-3), 124.39 (C-13), 127.46 (C-12), 128.49 (C-10), 131.65 (C-9), 132.86 (C-11), 137.36 (C-8), 168.77 (C-1), 202.14 ppm (C-4).

Synthesis of 5-bromo-6-bromomethylbenzo[1,3]dioxole (1c)[4]

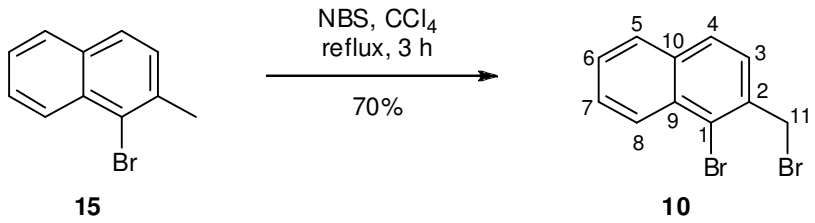


14 **1c**

An oven dried round-bottomed flask containing 15.0 g (98.7 mmol) piperonyl alcohol (**14**) and 30 mL acetic acid was at first cooled to 0 °C and then charged slowly with a mixture of 2.0 mL (116.4 mmol) Br_2 and 15 mL acetic acid. The reaction mixture was allowed to stirr at room temperature for 10 h. The precipitate was filtered, washed with distilled water and dried in *vacuo* to afford 26 g crude product. Recrystallization from MeOH delivered 25 g (88%) of 5-bromo-6-bromomethylbenzo[1,3]dioxole (**1c**) as a white solid.

M.**p**.: 92-93 °C (ref. [3] 91.5-92.5 °C); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 4.55 (s, 2H; 10-H_2), 5.99 (s, 2H; 2-H_2), 6.91 (s, 1H; 4-H), 7.01 (s, 1H; 7-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 34.08 (C-10), 102.05 (C-2), 110.47 (C-4), 113.08 (C-7), 115.59 (C-5), 129.9 (C-6), 147.58 (C-9), 148.74 ppm (C-8).

Synthesis of 1-bromo-2-(bromomethyl)naphthalene (10)[5]

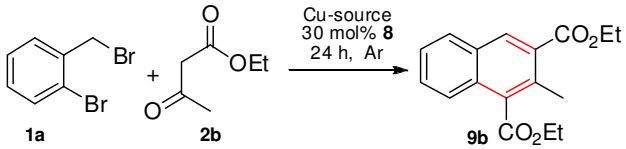


In an oven dried round-bottomed flask 5.0 g (16.7 mmol) 1-bromo-2-methyl-naphthalene (**15**) were dissolved in 100 mL CCl_4. Afterwards, 2.96 g (16.7 mmol) of *N*-bromosuccinimide and 3 mg of benzoyl peroxide were added. The reaction mixture was allowed to reflux for 3 h, cooled to room temperature and washed with 50 mL saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. Recrystallization from hexane afforded 3.6 g (70%) of 1-bromo-2-(bromomethyl)naphthalene (**10**) as a colourless solid.

M.p.: 103-104 °C (ref.[4] 103-105 °C); **^{1}H NMR** (300 MHz, $CDCl_3$): 4.87 (s, 2H; 11-H_2), 7.51-7.62 (m, 3H; 3-H, 6-H and 7-H), 7.78-7.83 (m, 2H; 4-H and 5-H), 8.34 (br d, ^3J (7-H, 8-H) = 8.7 Hz, 1H; 8-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 34.71 (C-11), 124.93 (C-1), 127.16 (C-8), 127.58 (C-7), 127.7 (C-3), 127.82 (C-6), 128.12 (C-4), 128.27 (C-5), 132.48 (C-2), 134.11 (C-9), 134.9 ppm (C-10).

6. Optimization of the Cu(I)-catalyzed synthesis of naphthalenes

Table 4. Optimization of the Cu(I)-catalyzed synthesis of naphthalene **9b**.[a]



1a **2b** **9b**

entry	Cu-source/ [mol%]	base [equiv.]	solvent	T [°C]	yield **9b** [%]
1	CuI/–	Cs_2CO_3/3	DMF	40	–
2	CuI/10	K_3PO_4/3	DMF	40	26[b]
3	CuI/10	K_2CO_3/3	DMF	40	19[b]
4	CuI/10	Cs_2CO_3/3	DMF	100	46[c]
5	CuI/10	Cs_2CO_3/4	DMF	100	52[c]
6	CuI/10	Cs_2CO_3/4	DMA	100	53[c]
7	CuI/10	Cs_2CO_3/4	MeCN	100	39[b]
8	CuI/10	Cs_2CO_3/4	DMSO	100	34[b]
9	**CuI/10**	**Cs_2CO_3/4**	**NMP**	**100**	**68**
10	CuI/20	Cs_2CO_3/4	NMP	100	69
11	CuI/5	Cs_2CO_3/4	NMP	100	37
12	Cu/10	Cs_2CO_3/4	DMF	100	10[b]
13	CuCl/10	Cs_2CO_3/4	DMF	100	15[b]
14	CuBr/10	Cs_2CO_3/4	DMF	100	21[b]

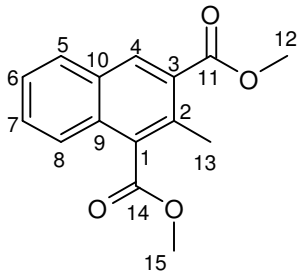
[a]Reactions were performed using 0.5 mmol **1a** and 1.5 mmol **2b** in sealed vial. [b]Traces of product **3b** were formed (TLC). [c]Product **3b** was formed in 3% yield.

7. General experimental procedure II for the Cu(I)-catalyzed synthesis of naphthalenes

An oven dried 10 mL vial was charged with 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%), 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) and 0.5 mmol of a 2-bromobenzyl bromide derivative **1**. The vial was sealed, evacuated and backfilled with argon (six times). 1.5 mmol freshly distilled β-ketoester **2** and 3 mL of *N*-methyl pyrrolidine were added using a syringe. Finally, the reaction mixture was heated in an oil bath at 100 °C for 24 h. After cooling to room temperature the reaction mixture was partitioned between 50 mL ethyl acetate and 20 mL brine. The aqueous phase was extracted with ethyl acetate (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in *vacuo*. The residue thus obtained was purified by flash column chromatography over silica gel (cyclohexane/EtOAc = 20:1).

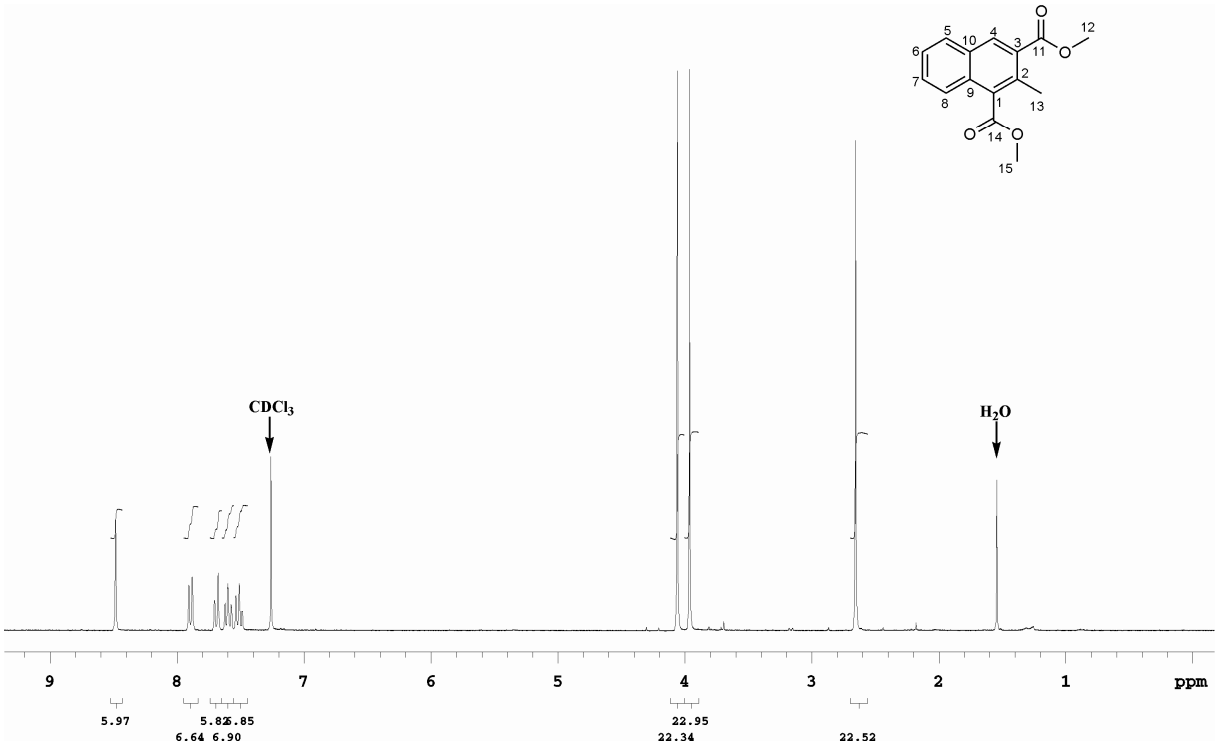
8. Synthesis and characterization of naphthalenes 9a-i

Synthesis of dimethyl-2-methylnaphthalene-1,3-dicarboxylate (9a)



9a

According to the general procedure II, 125 mg (0.5 mmol) 2-bromobenzyl bromide (**1a**), 174 mg (1.5 mmol) methyl acetoacetate (**2a**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 84 mg (65%) dimethyl-2-methylnaphthalene-1,3-dicarboxylate (**9a**) as a colourless oil.



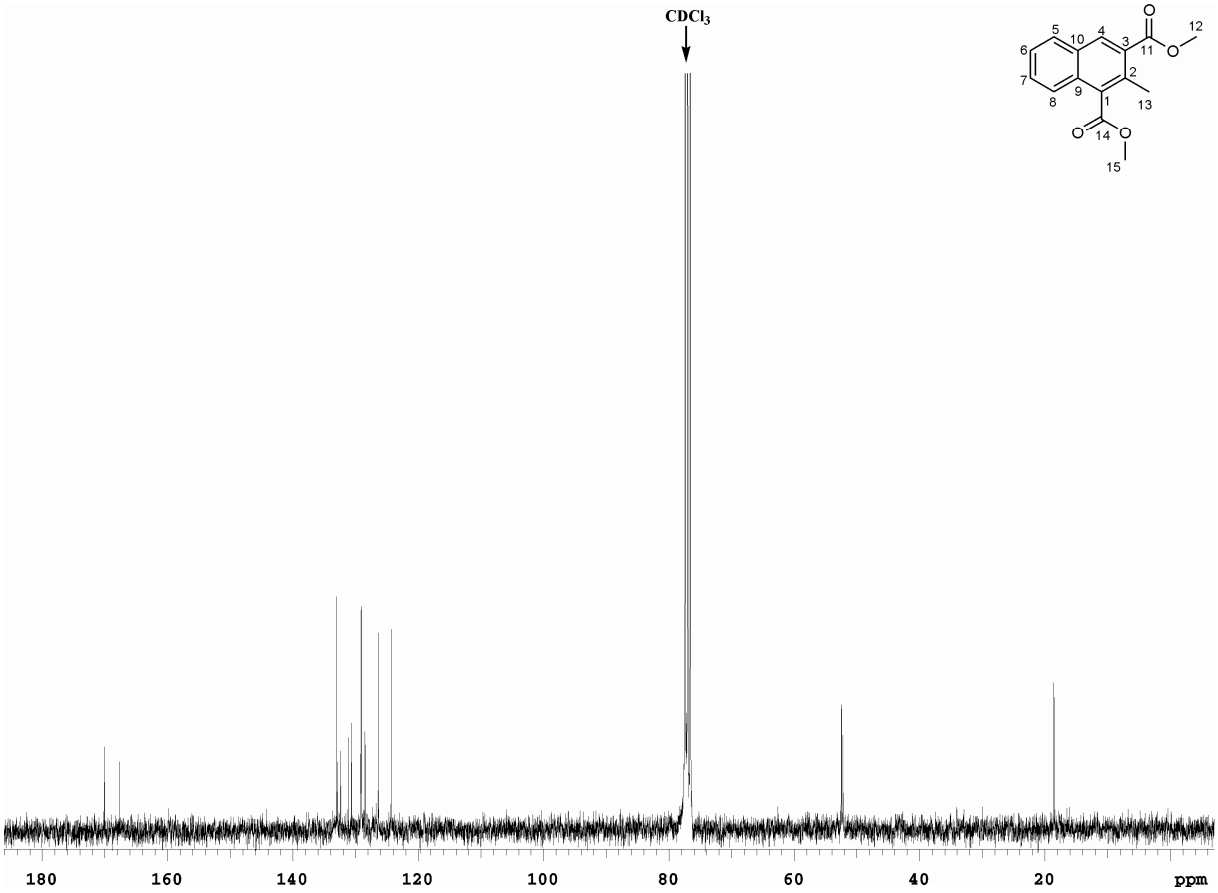
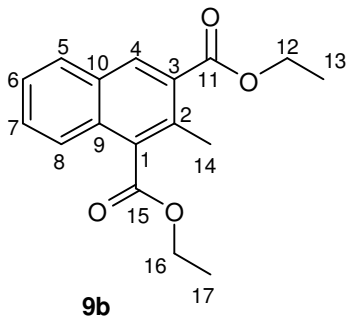


Figure 9. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9a** in $CDCl_3$.

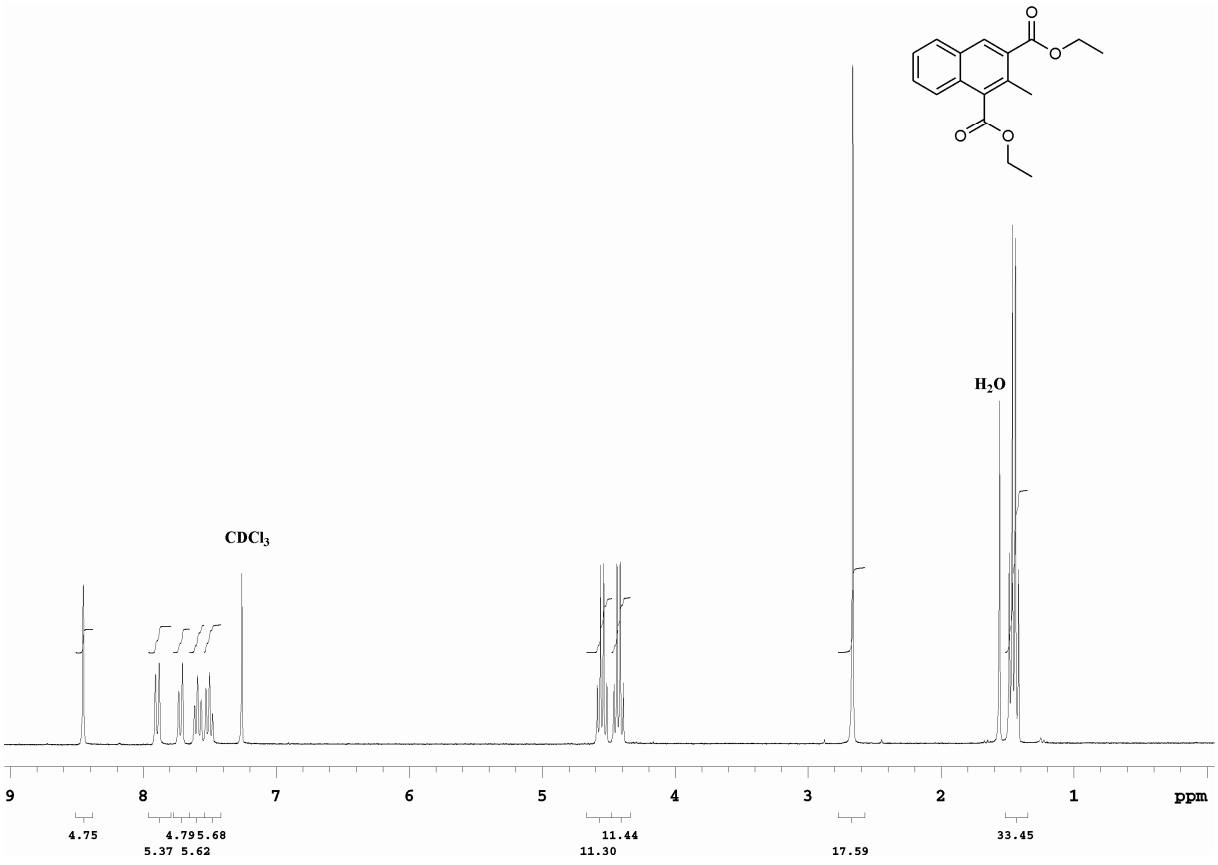
$\boldsymbol{R_f}$ = 0.49 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3100 (w; CH_3), 1712 (s; C=O), 1381 (m; alkane C-H), 1297 (m; ester C-O), 1240 (s; ester C-O), 1046 (s), 965 (m), 878 (m; arom. C-H), 855 (m; arom. C-H), 763 (s), 751 (s; alkane C-H), 735 cm^{-1} (w); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 234 (4.47), 282 nm (3.47); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.66 (s, 3H; 13-H_3), 3.96 (s, 3H; 12-H_3), 4.06 (s, 3H; 15-H_3), 7.54 (ddd, ^{3}J (6-H, 7-H) = 6.9 Hz, ^{3}J (5-H, 6-H) = 8.0 Hz, ^{4}J (6-H, 8-H) = 1.2 Hz, 1H; 6-H), 7.64 (ddd, ^{3}J (6-H, 7-H) = 7.0 Hz, ^{3}J (7-H, 8-H) = 7.1 Hz, ^{4}J (5-H, 7-H) = 1.4 Hz, 1H; 7-H), 7.73 (d, ^{3}J (7-H, 8-H) = 6.9 Hz, 1H; 8-H), 7.89 (br d, ^{3}J (5-H, 6-H) = 8.3 Hz, 1H; 5-H), 8.48 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 18.57 (C-13), 52.23 (C-12), 52.48 (C-15), 124.34 (C-8), 126.37 (C-6), 128.47 (C-3), 129.08 (C-5), 129.17 (C-7), 130.66 (C-10), 131.20 (C-9), 132.37 (C-2), 132.84 (C-4), 133.01 (C-1), 167.70 (C-11), 170.04 ppm (C-14); **MS** (EI, 70 eV): *m/z* (%) = 259 (14) $[M+1]^+$, 258 (100) $[M^+]$, 257 (14) $[M-1]^+$, 243 (14) $[M-CH_3]^+$, 227 (78) $[M-CO]^+$, 211 (10), 198 (72), 169 (15), 139 (28) $[C_{11}H_7]^+$, 128 (10), 98 (10); **HRMS** (EI, M^+) calculated for $C_{15}H_{14}O_4$: 258.0892; found: 258.0900.

Synthesis of diethyl-2-methylnaphthalene-1,3-dicarboxylate (9b)



9b

According to the general procedure II, 125 mg (0.5 mmol) 2-bromobenzyl bromide (**1a**), 195 mg (1.5 mmol) ethyl acetoacetate (**2b**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 98 mg (68%) diethyl-2-methylnaphthalene-1,3-dicarboxylate (**9b**) as a colourless oil.



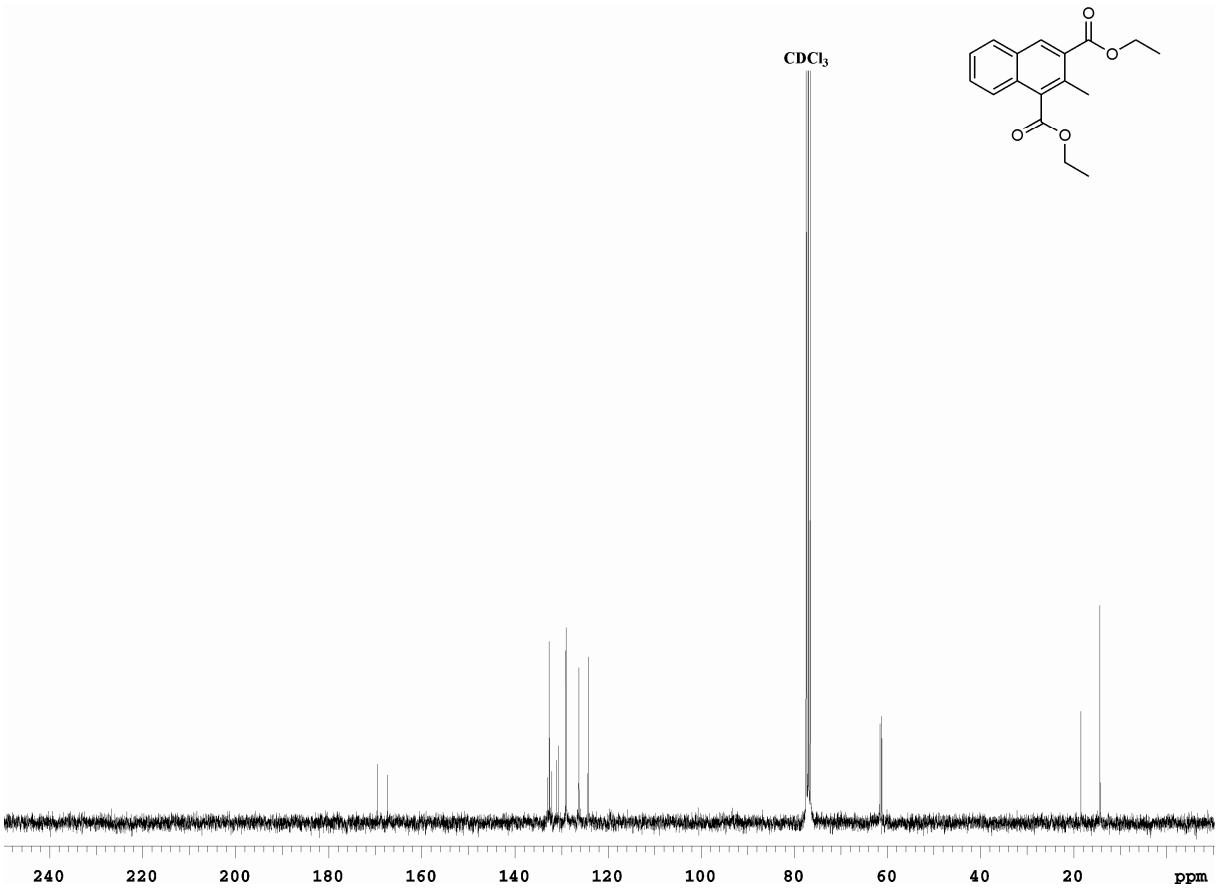
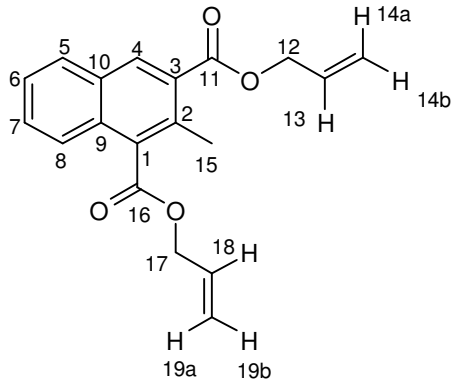


Figure 10. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9b** in $CDCl_3$.

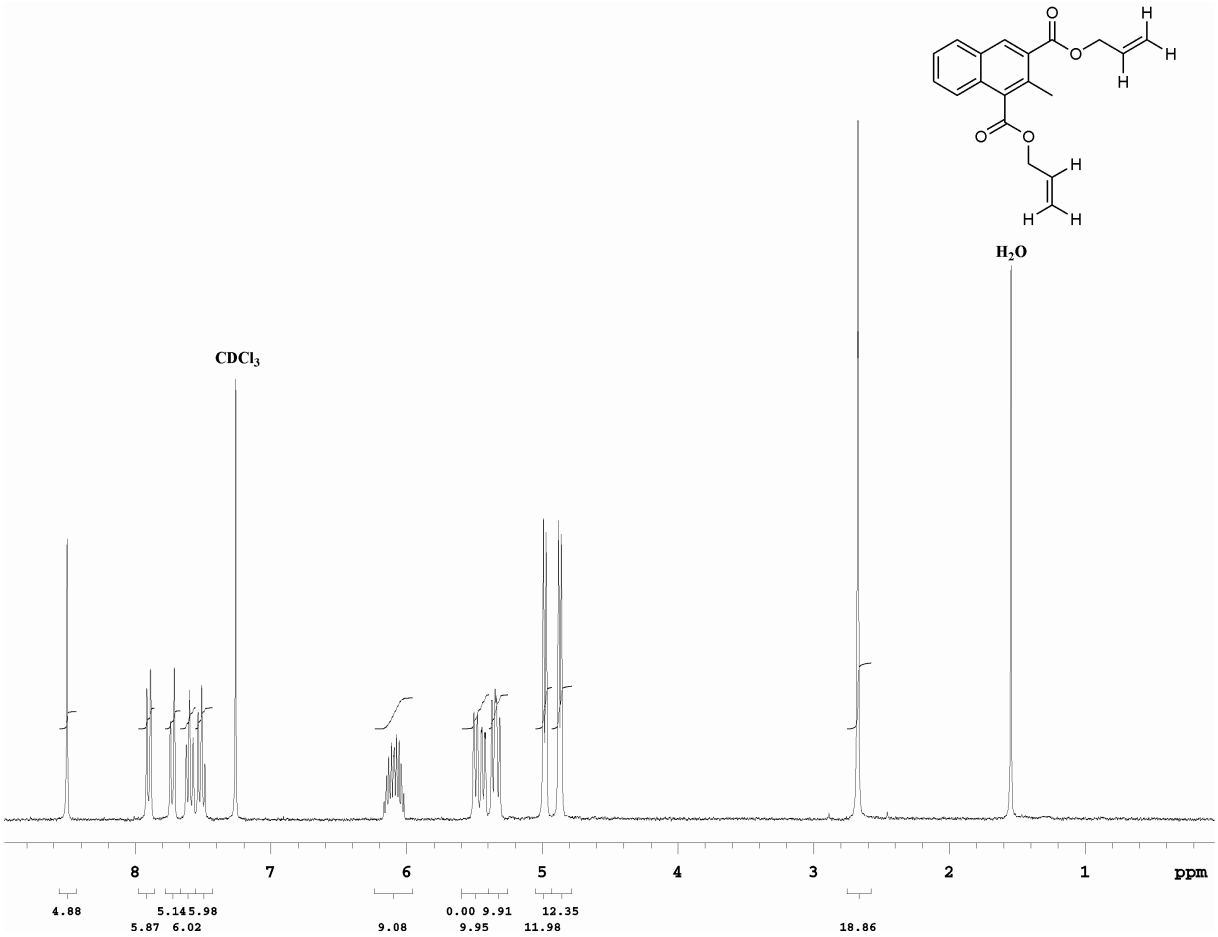
$\boldsymbol{R_f}$ = 0.43 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3100 (w; CH_2, CH_3), 1708 (s; C=O), 1379 (m; alkane C-H), 1297 (m; ester C-O), 1226 (s; ester C-O), 1046 (s), 1012 (m), 960 (m), 895 (m; arom. C-H), 850 (m; arom. C-H), 784 (s), 752 (s; alkane C-H), 735 cm^{-1} (w); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 233 (4.69), 282 (3.66), 335 nm (2.58); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.44 (t, ^{3}J (12-H, 13-H) = 6.9 Hz, 3H; 13-H_3), 1.46 (t, ^{3}J (16-H, 17-H) = 6.9 Hz, 3H; 17-H_3), 2.67 (s, 3H; 14-H_3), 4.42 (q, ^{3}J (12-H, 13-H) = 7.1 Hz, 2H; 12-H_2), 4.55 (q, ^{3}J (16-H, 17-H) = 7.2 Hz, 2H; 16-H_2), 7.50 (ddd, ^{3}J (6-H, 7-H) = 6.8 Hz, ^{3}J (5-H, 6-H) = 7.9 Hz, ^{4}J (6-H, 8-H) = 1.2 Hz, 1H; 6-H), 7.60 (ddd, ^{3}J (6-H, 7-H) = 6.9 Hz, ^{3}J (7-H, 8-H) = 6.9 Hz, ^{4}J (5-H, 7-H) = 1.4 Hz, 1H; 7-H), 7.72 (d, ^{3}J (7-H, 8-H) = 6.9 Hz, 1H; 8-H), 7.89 (br d, ^{3}J (5-H, 6-H) = 8.3 Hz, 1H; 5-H), 8.45 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.33 (C-13 and C-17), 18.43 (C-14), 61.2 (C-12), 61.6 (C-16), 124.28 (C-8), 126.28 (C-6), 129.0 (C-3), 129.01 (C-5), 129.04 (C-7), 130.69 (C-10), 131.10 (C-9), 132.05 (C-2), 132.63 (C-4), 133.0 (C-1), 167.39 (C-11), 169.59 ppm (C-15); **MS** (EI, 70 eV): *m/z* (%) = 287 (14) $[M+1]^+$, 286 (100) $[M^+]$, 257 (14) $[C_{16}H_{17}O_3]^+$, 241 $[C_{16}H_{17}O_2]^+$, 229 (32) $[C_{15}H_{17}O_2]^+$, 212 (63) $[C_{15}H_{16}O]^+$, 184 (24) $[C_{14}H_{16}]^+$, 139 (22) $[C_{11}H_7]^+$, 115 $[C_9H_5]^+$; **HRMS** (EI, M^+) calculated for $C_{17}H_{18}O_4$: 286.1205; found: 286.1177.

Synthesis of diallyl-2-methylnaphthalene-1,3-dicarboxylate (9c)



9c

According to the general procedure II, 125 mg (0.5 mmol) 2-bromobenzyl bromide (**1a**), 213 mg (1.5 mmol) allyl acetoacetate (**2e**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 107 mg (69%) diallyl-2-methylnaphthalene-1,3-dicarboxylate (**9c**) as a colourless oil.



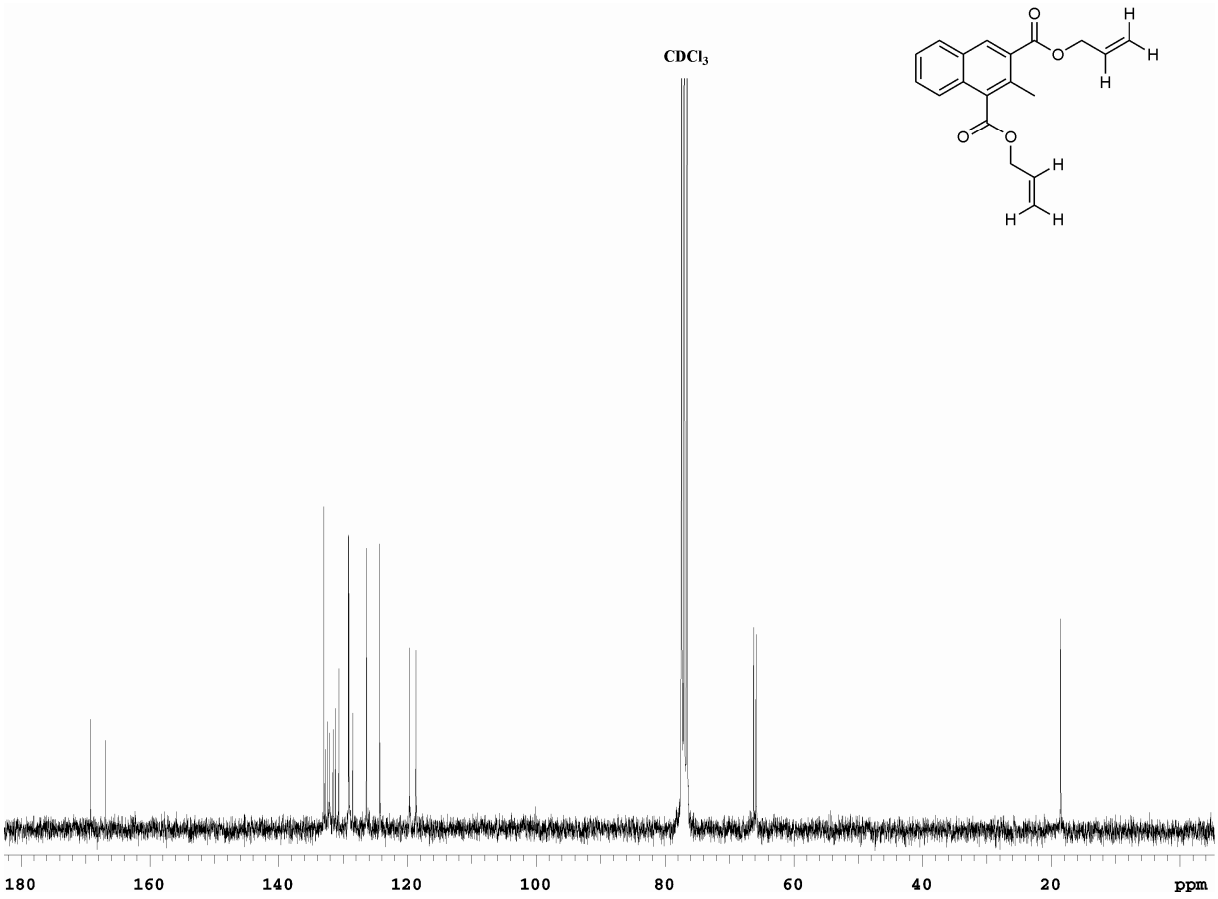
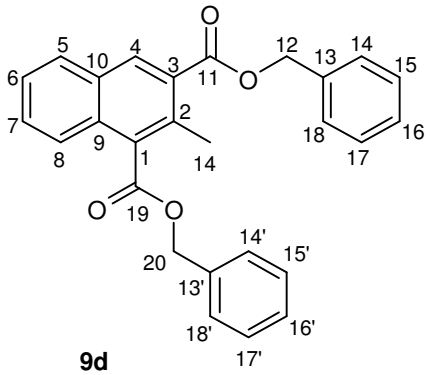


Figure 11. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9c** in $CDCl_3$.

$\boldsymbol{R_f}$ = 0.40 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2943 (w; CH_2, CH_3), 1716 (s; C=O), 1467 (m), 1438 (m), 1392 (w; alkane C-H), 1297 (m; ester C-O), 1228 (s; ester C-O), 1213 (s; ester C-O), 1046 (m), 1067 (m), 1045 (m), 991 (s), 938 (s; arom. C-H), 919 (s; arom. C-H) (s), 783 (s), 749 (s; alkane C-H) (s), 730 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 235 (4.75), 282 (3.72), 334 nm (2.62); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.67 (s, 3H; 15-H_3), 4.87 (ddd, ^{2}J (12-H, 12-H) = 1.6 Hz, ^{3}J (12-H, 13-H) = 5.7 Hz, ^{4}J (12-H, 14-H) = 1.3 Hz, 2H; 12-H_2), 4.98 (ddd, ^{2}J (17-H, 17-H) = 1.6 Hz, ^{3}J (17-H, 18-H) = 6.0 Hz, ^{4}J (17-H, 19-H) = 1.2 Hz, 2H; 17-H_2), 5.33 (ddt, ^{2}J (14a-H, 14b-H) = 1.4 Hz, $^{3}J_{cis}$ (13-H, 14b-H) = 10.4 Hz, ^{4}J (12-H, 14b-H) = 1.4 Hz, 1H; 14b-H), 5.35 (ddt, ^{2}J (19a-H, 19b-H) = 1.4 Hz, $^{3}J_{cis}$ (18-H, 19b-H) = 10.7 Hz, ^{4}J (17-H, 19b-H) = 1.2 Hz, 1H; 19b-H), 5.45 (ddt, ^{2}J (14a-H, 14b-H) = 1.4 Hz, $^{3}J_{trans}$ (13-H, 14a-H) = 17.4 Hz, ^{4}J (12-H, 14a-H) = 1.4 Hz, 1H; 14a-H), 5.47 (ddt, ^{2}J (19a-H, 19b-H) = 1.4 Hz, $^{3}J_{trans}$ (18-H, 19a-H) = 17.2 Hz, ^{4}J (17-H, 19a-H) = 1.4 Hz, 1H; 19a-H), 6.06 (m, 1H; 13-H), 6.11 (m, 1H; 18-H), 7.51 (ddd, ^{3}J (6-H, 7-H) = 6.9 Hz, ^{3}J (5-H, 6-H) = 7.7 Hz, ^{4}J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.60 (ddd, ^{3}J (6-H, 7-H) = 6.9 Hz, ^{3}J (7-H, 8-H) = 8.4 Hz, ^{4}J (5-H, 7-H) = 1.5 Hz, 1H; 7-H), 7.73 (br d, ^{3}J (7-H, 8-H) = 8.1 Hz, 1H; 8-H), 7.90 (br d, ^{3}J (5-H, 6-H) = 8.1 Hz, 1H; 5-H), 8.50 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 18.55 (C-15), 65.85 (C-12), 66.21 (C-17), 118.67 (C-14), 119.65 (C-19), 124.31 (C-8), 126.36 (C-6),

128.51 (C-3), 129.1 (C-5), 129.18 (C-7), 130.67 (C-10), 131.22 (C-9), 131.56 (C-18), 132.08 (C-13), 132.35 (C-2), 132.73 (C-1), 132.98 (C-4), 166.88 (C-11), 169.21 ppm (C-16); **MS** (EI, 70 eV): *m/z* (%) = 311 (7) $[M+1]^+$, 310 (36) $[M^+]$, 269 (52) $[C_{16}H_{13}O_4]^+$, 253 (64) $[C_{16}H_{13}O_3]^+$, 227 (84) $[C_{14}H_{11}O_3]^+$, 211 (72) $[C_{14}H_{11}O_2]^+$, 181 (64) $[C_{13}H_9O]^+$, 139 (100) $[C_{11}H_7]^+$, 115 (24) $[C_9H_7]^+$; **HRMS** (EI, M^+) calculated for $C_{19}H_{18}O_4$: 310.1206; found: 310.1197.

Synthesis of dibenzyl-2-methylnaphthalene-1,3-dicarboxylate (9d)



9d

According to the general procedure II, 125 mg (0.5 mmol) 2-bromobenzyl bromide (**1a**), 288 mg (1.5 mmol) benzyl acetoacetate (**2c**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 134 mg (65%) dibenzyl-2-methylnaphthalene-1,3-dicarboxylate (**9d**) as a colourless oil.

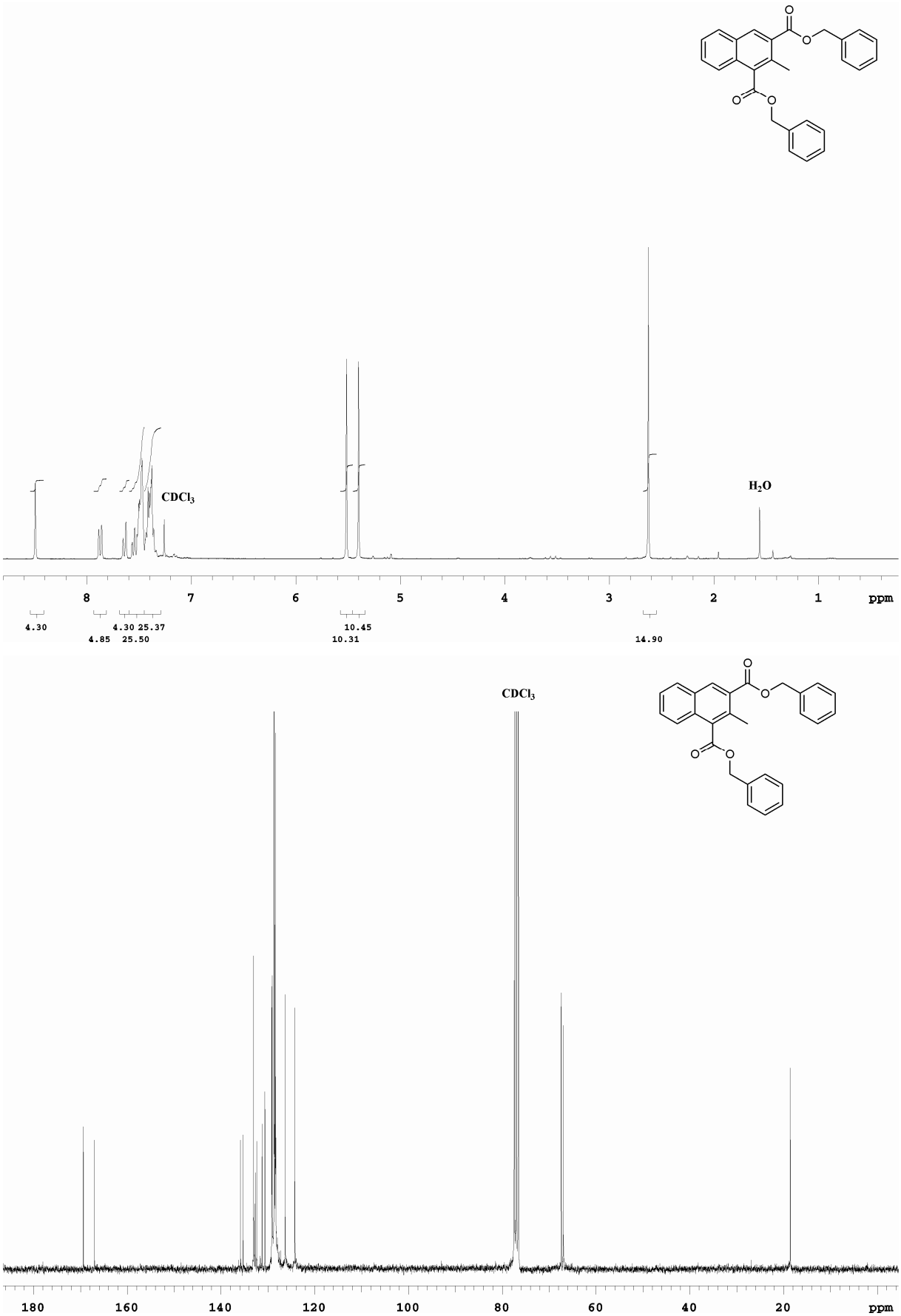
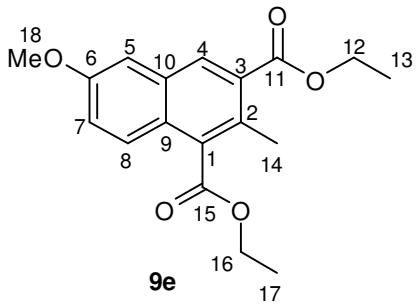


Figure 12. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9d** in $CDCl_3$.

R_f = 0.41 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3031 (w; CH_2, CH_3), 2955 (w; CH_2, CH_3), 1712 (s; C=O), 1497 (m), 1455 (m), 1358 (m; alkane C-H), 1296 (m; ester C-O), 1196 (s; ester C-O), 1139 (s; ester C-O), 1062 (m), 1042 (m), 1027 (m), 973 (m; arom. C-H), 909 (m; arom. C-H), 789 (m), 747 (s; alkane C-H), 696 cm^{-1} (s); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 235 nm (4.32); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.63 (s, 3H; 14-H_3), 5.40 (s, 2H; 12-H_2), 5.52 (s, 2H; 20-H_2), 7.47 (overlapped, 1H; 6-H), 7.50-7.53 (overlapped, 10H; 14-H, 14'-H, 15-H, 15'-H, 16-H, 16'-H, 17-H, 17'-H, 18-H and 18'-H), 7.54 (ddd, ^3J (6-H, 7-H) = 6.9 Hz, ^3J (7-H, 8-H) = 8.5 Hz, ^4J (5-H, 7-H) = 1.6 Hz, 1H; 7-H), 7.64 (br d, ^3J (7-H, 8-H) = 8.4 Hz, 1H; 8-H), 7.87 (br d, ^3J (5-H, 6-H) = 8.4 Hz, 1H; 5-H), 8.49 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 18.56 (C-14), 66.97 (C-12), 67.41 (C-20), 124.26 (C-8), 126.32 (C-6), 128.33 (C-14 and C-18), [128.35, 128.40, 128.42, 128.56, 128.66 (overlapped, C-3, C-15, C-15', C-16, C-16', C-17, C-17')], 128.71 (C-14' and C-18'), 129.09 (C-5), 129.16 (C-7), 130.62 (C-10), 131.23 (C-9), 132.39 (C-1), 132.69 (C-2), 133.04 (C-4), 135.29 (C-13'), 135.85 (C-13), 167.01 (C-11), 169.34 ppm (C-19); **MS** (EI, 70 eV): *m/z* (%) = 411 (6) $[M+1]^+$, 410 (22) $[M^+]$, 319 (78) $[M–C_7H_7]^+$, 310 (57) $[C_{20}H_{13}O_3]^+$, 283 (13) $[C_{20}H_{11}O_2]^+$, 229 (6), 139 (8) $[C_{11}H_7]^+$, 91 (100) $[C_7H_7]^+$; **HRMS** (EI, M^+) calculated for $C_{27}H_{22}O_4$: 410.1519; found: 410.1541.

Synthesis of diethyl-6-methoxy-2-methylnaphthalene-1,3-dicarboxylate (9e)



9e

According to the general procedure II, 140 mg (0.5 mmol) 2-bromo-5-methoxybenzyl bromide (**1b**), 195 mg (1.5 mmol) ethyl acetoacetate (**2b**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 119 mg (76%) diethyl-6-methoxy-2-methylnaphthalene-1,3-dicarboxylate (**9e**) as a colourless oil.

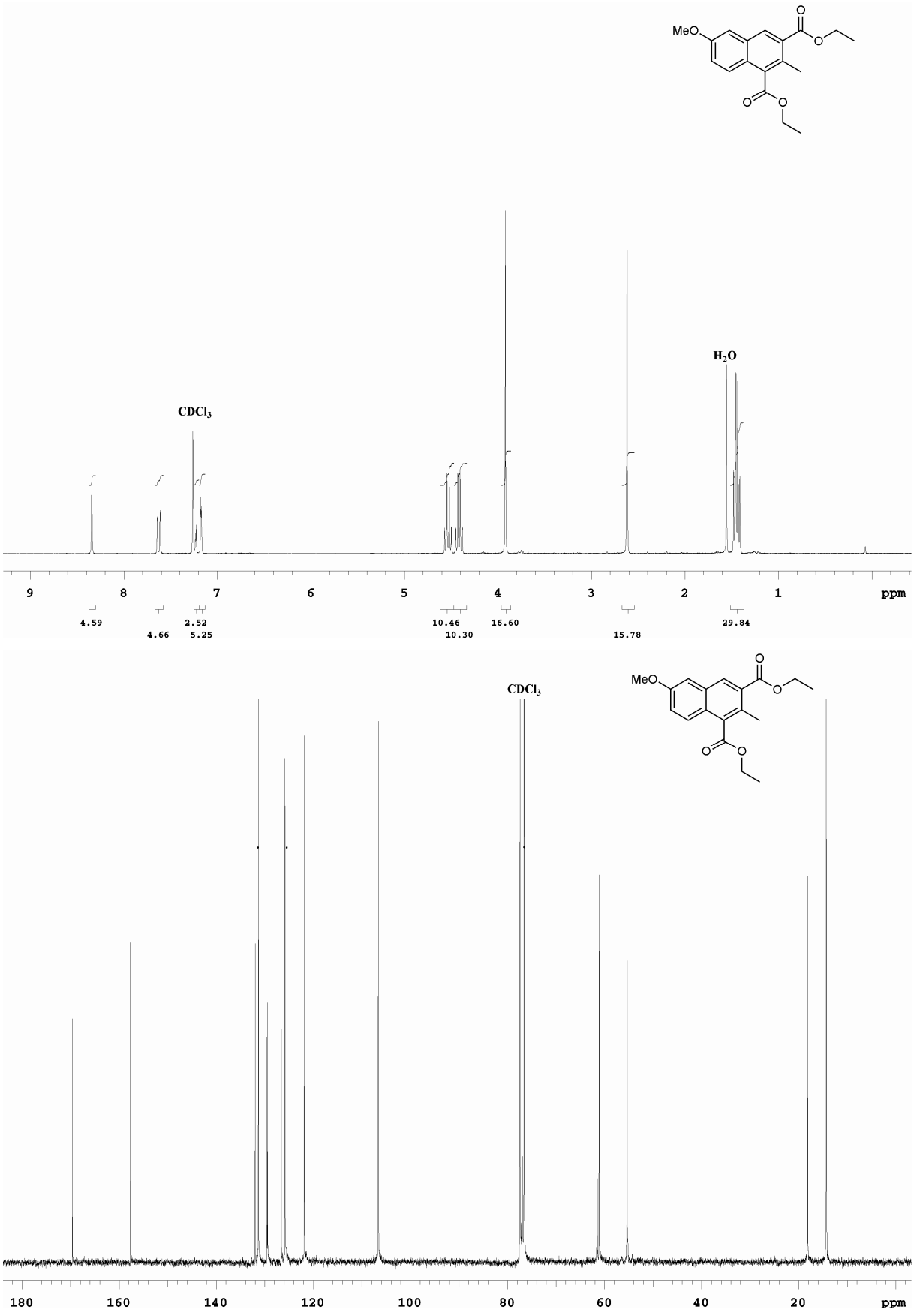
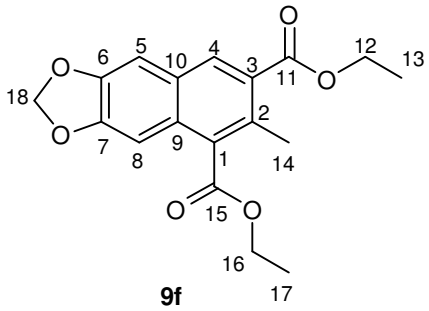


Figure 13. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9e** in $CDCl_3$.

R_f = 0.46 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2981 (m; CH_2, CH_3), 1714 (s; C=O), 1599 (m), 1466 (m), 1363 (m; alkane C-H), 1293 (m; ester C-O), 1231 (s; ester C-O), 1152 (s; ester C-O), 1041 (s), 1017 (s), 859 (m; arom. C-H), 780 (m), 697 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 238 nm (4.28); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.43 (t, ^3J (12-H, 13-H) = 7.1 Hz, 3H; 13-H_3), 1.45 (t, ^3J (16-H, 17-H) = 7.1 Hz, 3H; 17-H_3), 2.36 (s, 3H; 14-H_3), 3.92 (s, 3H; 18-H_3), 4.41 (q, ^3J (12-H, 13-H) = 7.1 Hz, 2H; 12-H_2), 4.53 (q, ^3J (16-H, 17-H) = 7.1 Hz, 2H; 16-H_2), 7.17 (d, ^4J (5-H, 7-H) = 2.5 Hz, 1H; 5-H), 7.24 (dd, ^3J (7-H, 8-H) = 9.1 Hz, ^4J (5-H, 7-H) = 2.7 Hz, 1H; 7-H), 7.62 (d, ^3J (7-H, 8-H) = 9.1 Hz, 1H; 8-H), 8.34 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.3 (C-13 and C-17), 18.14 (C-14), 55.35 (C-18), 61.11 (C-12), 61.54 (C-16), 106.61 (C-5), 121.86 (C-7), 125.83 (C-8), 126.61 (C-9), 129.43 (C-3), 129.57 (C-2), 131.31 (C-4), 132.0 (C-10), 132.86 (C-1), 157.7 (C-6), 167.51 (C-11), 169.65 ppm (C-15); **MS** (EI, 70 eV): *m/z* (%) = 317 (18) $[M+1]^+$, 316 (100) $[M^+]$, 271 (43) $[C_{16}H_{15}O_4]^+$, 259 (24), 242 (82) $[C_{15}H_{15}O_3]^+$, 214 (32) $[C_{14}H_{15}O_2]^+$, 170 (6), 127 (7), 77 (2) $[C_6H_5]^+$; **HRMS** (EI, M^+) calculated for $C_{18}H_{20}O_5$: 316.1311; found: 316.1315.

Synthesis of diethyl-2-methyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (9f)



9f

According to the general procedure II, 147 mg (0.5 mmol) 2-bromo-4,5-methylenedioxybenzyl bromide (**1c**), 195 mg (1.5 mmol) ethyl acetoacetate (**2b**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 116 mg (70%) diethyl-2-methyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (**9f**) as a colourless oil.

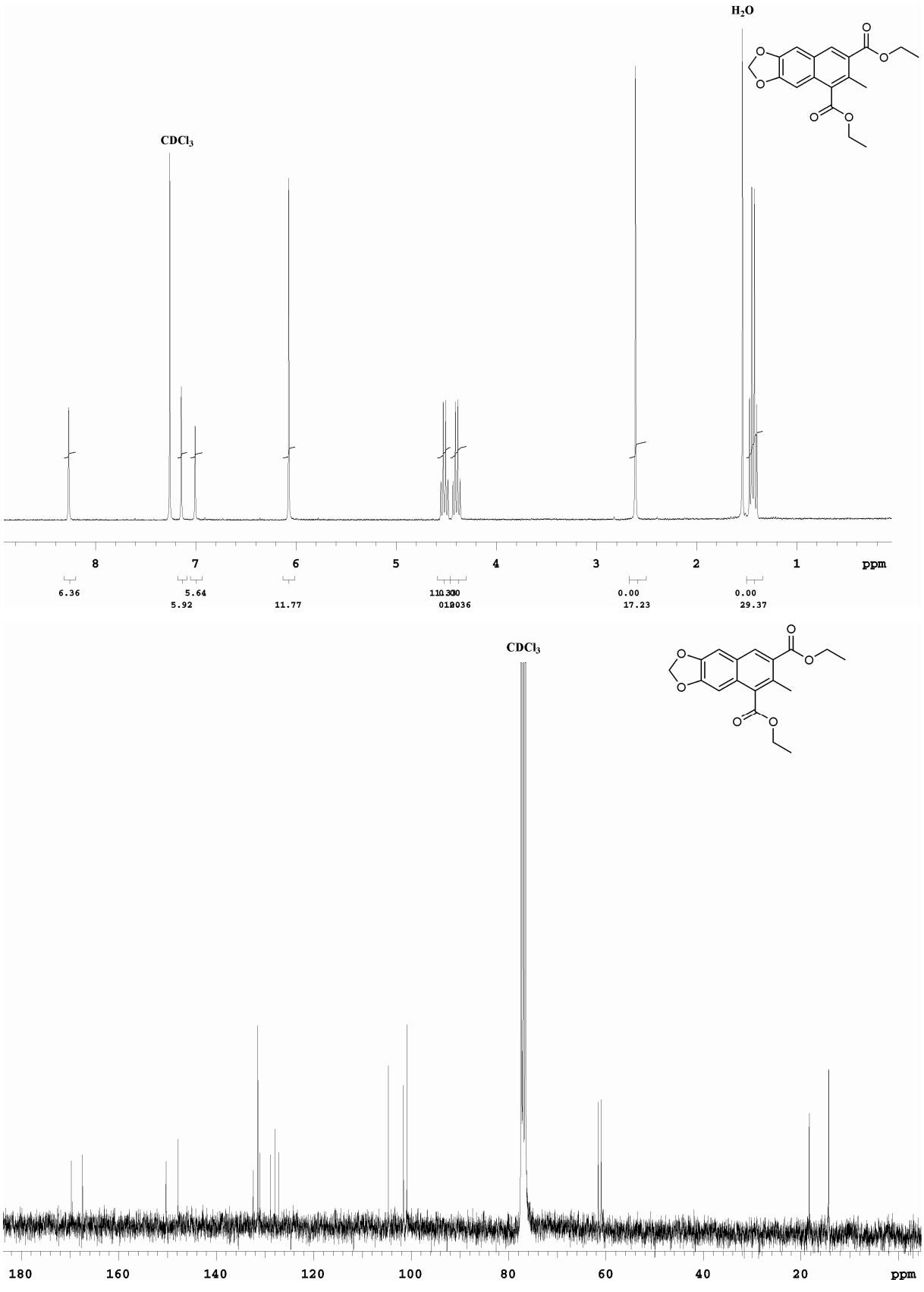
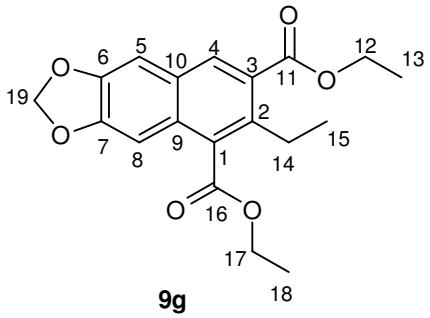


Figure 14. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9f** in $CDCl_3$.

***R*$_f$** = 0.42 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2963 (w; CH_2, CH_3), 2906 (w; CH_2, CH_3), 1704 (s; C=O), 1490 (m), 1458 (m), 1366 (w; alkane C-H), 1243 (s; ester C-O), 1204 (s; ester C-O), 1076 (m), 1035 (s), 943 (m; arom. C-H), 925 (m; arom. C-H), 803 (s; alkane C-H), 696 cm^{-1} (s); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 290 (3.82), 331 nm (3.07); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.43 (t, ^3J (12-H, 13-H) = 7.1 Hz, 3H; 13-H_3), 1.44 (t, ^3J (16-H, 17-H) = 7.0 Hz, 3H; 17-H_3), 2.61 (s, 3H; 14-H_3), 4.39 (q, ^3J (12-H, 13-H) = 7.1 Hz, 2H; 12-H_2), 4.52 (q, ^3J (16-H, 17-H) = 7.1 Hz, 2H; 16-H_2), 6.07 (s, 2H; 18-H_2), 7.01 (s, 1H; 8-H), 7.14 (s, 1H; 5-H), 8.27 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.33 (C-13 and C-17), 18.32 (C-14), 61.03 (C-12), 61.59 (C-16), 100.9 (C-8), 101.58 (C-18), 104.68 (C-5), 127.19 (C-3), 127.91 (C-10), 128.89 (C-9), 130.99 (C-2), 131.47 (C-4), 132.39 (C-1), 147.81 (C-6), 150.29 (C-7), 167.44 (C-11), 169.77 ppm (C-15); **MS** (EI, 70 eV): *m/z* (%) = 331 (16) [*M*+1]$^+$, 330 (88) [M^+], 301 (7) [*M*–Et]$^+$, 285 (62) $[C_{16}H_{13}O_5]^+$, 273 (82) $[C_{15}H_{13}O_5]^+$, 256 (100) $[C_{15}H_{12}O_4]^+$, 228 (44) $[C_{14}H_{12}O_3]^+$, 199 (20) $[C_{13}H_{11}O_2]^+$, 184 (30) $[C_{12}H_8O_2]^+$, 171 (11), 143 (10), 126 (22), 115 (24) $[C_9H_7]^+$, 77 (10) $[C_6H_5]^+$; **HRMS** (EI, M^+) calculated for $C_{18}H_{18}O_6$: 330.1103; found: 330.1092.

Synthesis of Diethyl-2-ethyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (9g)



9g

According to the general procedure II, 147 mg (0.5 mmol) 2-bromo-4,5-methylenedioxybenzyl bromide (**1c**), 216 mg (1.5 mmol) ethyl propionylacetate (**2g**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 126 mg (73%) diethyl-2-ethyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (**9g**) as a colourless oil.

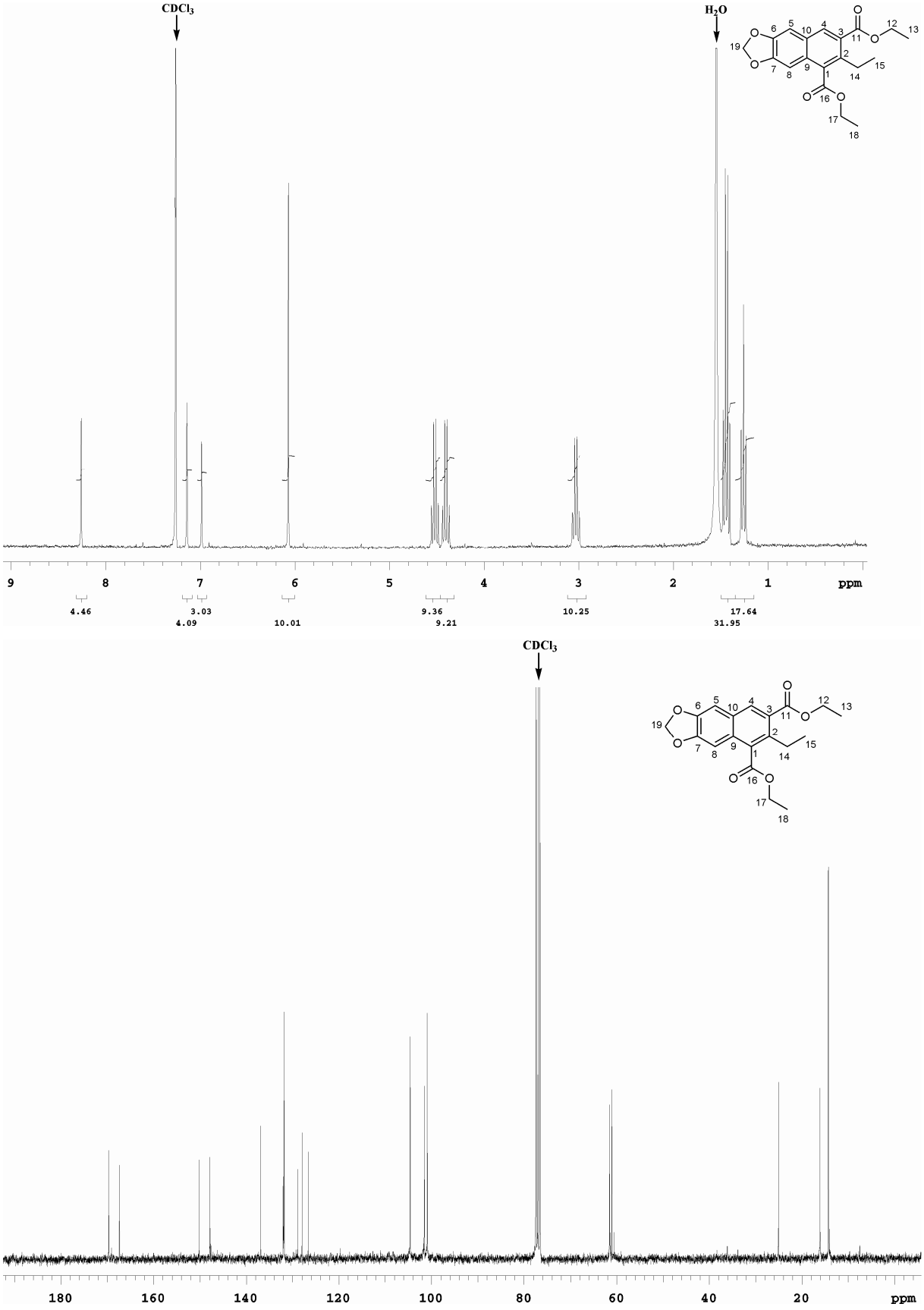
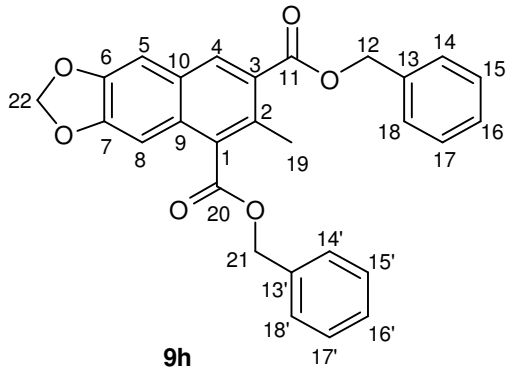


Figure 15. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9g** in $CDCl_3$.

R_f = 0.43 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2979 (w; CH_2, CH_3), 2904 (w; CH_2, CH_3), 1713 (s; C=O), 1497 (m), 1503 (m), 1479 (s), 1462 (s), 1368 (m; alkane C-H), 1242 (s; ester C-O), 1196 (s; ester C-O), 1070 (m), 1035 (s), 932 (m; arom. C-H), 861 (m; arom. C-H), 808 (m), 766 cm^{-1} (w; alkane C-H); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 248 (4.29), 291 nm (3.73); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.26 (t, ^3J (14-H, 15-H) = 7.5 Hz, 3H; 15-H_3), 1.43 (t, ^3J (12-H, 13-H) = 7.2 Hz, 3H; 13-H_3), 1.45 (t, ^3J (17-H, 18-H) = 7.1 Hz, 3H; 18-H_3), 3.04 (t, ^3J (14-H, 15-H) = 7.5 Hz, 2H; 14-H_2), 4.39 (q, ^3J (12-H, 13-H) = 7.1 Hz, 2H; 12-H_2), 4.53 (q, ^3J (17-H, 18-H) = 7.1 Hz, 2H; 17-H_2), 6.07 (s, 2H; 19-H_2), 6.99 (s, 1H; 8-H), 7.14 (s, 1H; 5-H), 8.26 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.29 (C-13 and C-18), 16.10 (C-15), 25.06 (C-14), 61.06 (C-12), 61.55 (C-17), 100.92 (C-8), 101.55 (C-19), 104.62 (C-5), 126.65 (C-3), 127.98 (C-10), 128.92 (C-9), 131.84 (C-2), 131.94 (C-4), 136.90 (C-1), 147.85 (C-6), 150.21 (C-7), 167.42 (C-11), 169.72 ppm (C-16); **MS** (EI, 70 eV): *m/z* (%) = 345 (18) $[M+1]^+$, 344 (100) $[M^+]$, 315 (32) $[M–Et]^+$, 299 (38) $[C_{17}H_{15}O_5]^+$, 287 (42), 270 (44), 213 (12), 175 (44), 135 (26), 115 (24) $[C_9H_7]^+$; **HRMS** (EI, M^+) calculated for $C_{19}H_{20}O_6$: 344.1259; found: 344.1286.

Synthesis of dibenzyl-2-methyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (9h)



9h

According to the general procedure II, 147 mg (0.5 mmol) 2-bromo-4,5-methylenedioxybenzyl bromide (**1c**), 288 mg (1.5 mmol) benzyl acetoacetate (**2c**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 182 mg (80%) dibenzyl-2-methyl-6,7-methylenedioxy-naphthalene-1,3-dicarboxylate (**9h**) as a pale yellow solid.

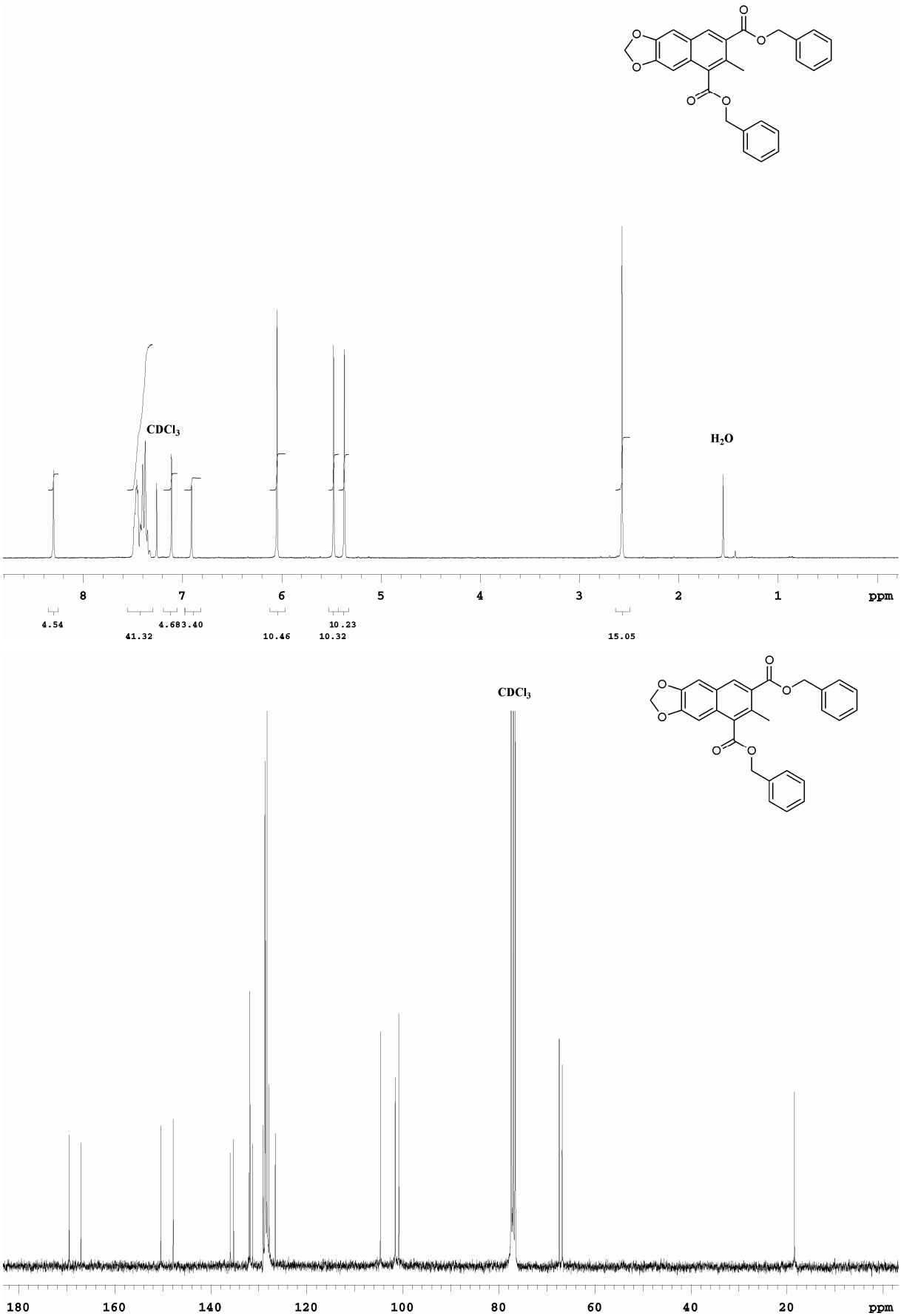
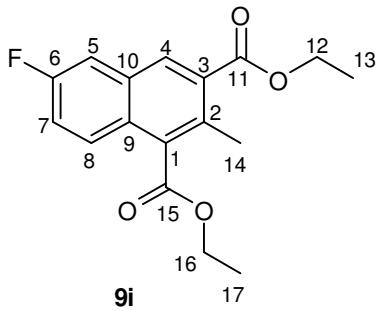


Figure 16. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9h** in $CDCl_3$.

M.p. = 151-152 °C; R_f = 0.40 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 1710 (s; C=O), 1497 (m), 1463 (m), 1316 (m; alkane C-H), 1270 (m; ester C-O), 1247 (s; ester C-O), 1203 (s; ester C-O), 1073 (m), 1032 (s), 938 (m; arom. C-H), 914 (m; arom. C-H), 849 (m), 753 (s; alkane C-H), 701 cm^{-1} (s); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 250 (4.54), 293 nm (3.70); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.57 (s, 3H; 19-H_3), 5.37 (s, 2H; 12-H_2), 5.48 (s, 2H; 21-H_2), 6.05 (s, 2H; 22-H_2), 6.91 (s, 1H; 8-H), 7.11 (s, 1H; 5-H), 7.32-7.50 (overlapped, 10H; 14-H, 14'-H, 15-H, 15'-H, 16-H, 16'-H, 17-H, 17'-H, 18-H and 18'-H), 8.30 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 18.45 (C-19), 66.82 (C-12), 67.43 (C-21), 100.84 (C-8), 101.59 (C-22), 104.69 (C-5), 126.58 (C-3), 127.85 (C-10), 128.30 (C-14 and C-18), [128.30, 128.59, 128.68, 128.69 (overlapped, C-15, C-15', C-16, C-16', C-17, C-17', C-18 and C-18')], 128.74 (C-14' and C-18'), 129.09 (C-9), 131.33 (C-2), 131.84 (C-4), 132.03 (C-1), 135.24 (C-13), 135.97 (C-13'), 147.85 (C-6), 150.41 (C-7), 167.05 (C-11), 169.53 ppm (C-20); **MS** (EI, 70 eV): *m/z* (%) = 455 (3) $[M+1]^+$, 454 (10) $[M^+]$, 363 (93) $[M- C_7H_7]^+$, 345 (5) $[C_{21}H_{13}O_5]^+$, 327 (2) $[C_{20}H_{13}O_4]^+$, 273 (3), 213 (2), 184 (3), 126 (3), 91 (70) $[C_7H_7]^+$; **HRMS** (EI, M^+) calculated for $C_{28}H_{22}O_6$: 454.1428; found: 454.1433.

Synthesis of diethyl-6-fluoro-2-methyl-naphthalene-1,3-dicarboxylate (9i)



9i

According to the general procedure II, 134 mg (0.5 mmol) 2-bromo-5-flourobenzyl bromide (**1d**), 195 mg (1.5 mmol) ethyl acetoacetate (**2b**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 104 mg (68%) diethyl-6-fluoro-2-methyl-naphthalene-1,3-dicarboxylate (**9i**) as a colourless oil.

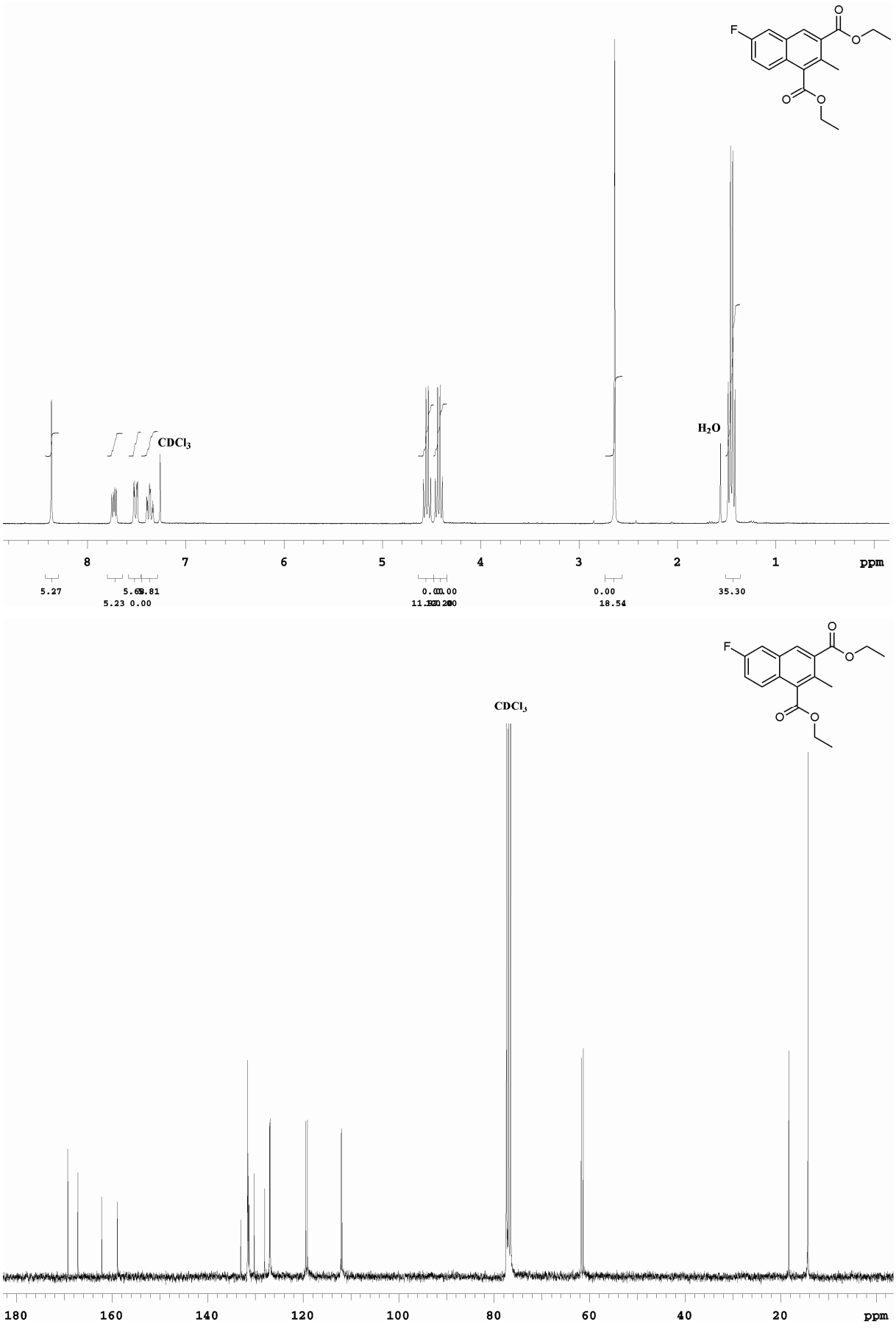
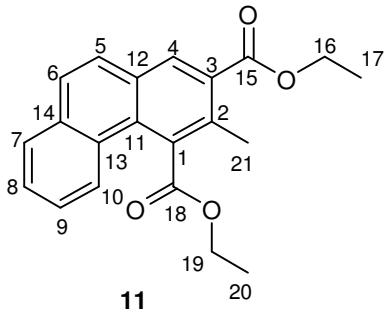


Figure 17. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9i** in $CDCl_3$.

R_f = 0.45 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2979 (w; CH_2, CH_3), 1728 (s; C=O), 1713 (s; C=O), 1507 (m), 1479 (m), 1452 (s), 1383 (m; alkane C-H), 1326 (m; alkane C-H), 1282 (m; ester C-O), 1207 (s; ester C-O), 1153 (m), 1129 (m), 1071 (m), 1045 (s), 1013 (m), 914 (m; arom. C-H), 854 (m; arom. C-H), 828 (m), 779 (w; alkane C-H), 769 cm^{-1} (w; alkane C-H); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 238 (4.68), 231 (4.68), 277 (3.78), 328 nm (3.05); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.44 (t, ^3J (12-H, 13-H) = 7.2 Hz, 3H; 13-H_3), 1.46 (t, ^3J (16-H, 17-H) = 7.2 Hz, 3H; 17-H_3), 2.64 (s, 3H; 14-H_3), 4.43 (q, ^3J (12-H, 13-H) = 7.4 Hz, 2H; 12-H_2), 4.55 (q, ^3J (16-H, 17-H) = 7.4 Hz, 2H; 16-H_2), 7.36 (ddd, ^3J (7-H, 8-H) = 9.3 Hz, ^3J (6-F, 7-H) = 8.3 Hz, ^4J (5-H, 7-H) = 2.5 Hz, 1H; 7-H), 7.51 (dd, ^3J (5-H, 6-F) = 9.1 Hz, ^4J (5-H, 7-H) = 2.6 Hz, 1H; 5-H), 7.73 (dd, ^3J (7-H, 8-H) = 9.4 Hz, ^4J (6-F, 8-H) = 5.5 Hz, 1H; 8-H), 8.36 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.3 (C-13 and C-17), 18.28 (C-14), 61.35 (C-12), 61.74 (C-16), 112,0 (d, ^2J (C-5, 6-F) = 19.8 Hz, C-5), 119.3 (d, ^2J (C-7, 6-F) = 25.2 Hz, C-7), 126.96 (d, ^3J (C-8, 6-F) = 8.9 Hz, C-8), 128.1 (d, ^4J (C-9, 6-F) = 1.0 Hz, C-9), 130.26 (C-3), 131.37 (C-2), 131.51 (C-10), 131.60 (C-4), 133.1 (br s, C-1), 160.55 (d, J (C-6, 6-F) = 247.9 Hz, C-6), 167.17 (C-11), 169.27 ppm (C-15); **MS** (EI, 70 eV): *m/z* (%) = 305 (14) $[M+1]^+$, 304 (92) $[M^+]$, 276 (12) $[M–CO]^+$, 259 (71), 248 (48), 230 (100), 202 (42), 157 (25), 146 (12), 133 (5); **HRMS** (EI, M^+) calculated for $C_{17}H_{17}FO_4$: 304.1111; found: 304.1109.

9. Synthesis of diethyl-2-methyl-phenanthrene-1,3-dicarboxylate (11)



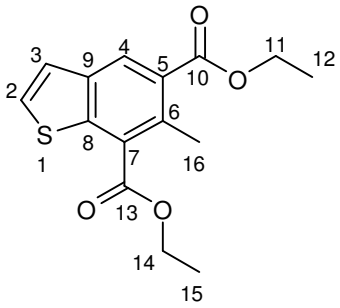
11

According to the general procedure II, 150 mg (0.5 mmol) 1-bromo-2-bromomethyl-naphthalene (**10**), 195 mg (1.5 mmol) ethyl acetoacetate (**2b**), 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%) and 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) were reacted in 3 mL *N*-methyl pyrrolidine in a sealed vial in an argon atmosphere at 100 °C for 24 h. Column chromatography over silicagel (cyclohexane/EtOAc = 20:1) afforded 116 mg (69%) diethyl-2-methyl-phenanthrene-1,3-dicarboxylate (**11**) as a pale yellow solid.

Figure 18. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **11** in $CDCl_3$.

M.p. = 102-104 °C; R_f = 0.46 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 3054 (w; CH_2, CH_3), 2980 (w; CH_2, CH_3), 1713 (s; C=O), 1503 (m), 1444 (m), 1367 (m; alkane C-H), 1215 (m; ester C-O), 1140 (s; ester C-O), 1093 (m), 1045 (s), 1018 (m), 964 (s; arom. C-H), 857 (m; arom. C-H), 810 (s), 767 (s; alkane C-H), 743 cm^{-1} (s; alkane C-H); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 271 nm (4.03); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.42 (t, ^3J (16-H, 17-H) = 6.9 Hz, 3H; 17-H_3), 1.46 (t, ^3J (19-H, 20-H) = 6.9 Hz, 3H; 20-H_3), 2.72 (s, 3H; 21-H_3), 4.45 (q, ^3J (16-H, 17-H) = 6.9 Hz, 2H; 16-H_2), 4.59 (q, ^3J (19-H, 20-H) = 6.9 Hz, 2H; 20-H_2), 7.58 (ddd, ^3J (8-H, 9-H) = 7.0 Hz, ^3J (9-H, 10-H) = 7.0 Hz, ^4J (7-H, 9-H) = 1.6 Hz, 1H; 9-H), 7.64 (ddd, ^3J (7-H, 8-H) = 7.4 Hz, ^3J (8-H, 9-H) = 7.4 Hz, ^4J (8-H, 10-H) = 1.2 Hz, 1H; 8-H), 7.72 (d, ^3J (5-H, 6-H) = 8.8 Hz, 1H; 5-H), 7.76 (d, ^3J (5-H, 6-H) = 8.0 Hz, 1H; 6-H), 7.91 (br d, ^3J (7-H, 8-H) = 7.1 Hz, 1H; 7-H), 8.43 (s, 1H; 4-H), 8.47 (br d, ^3J (9-H, 10-H) = 8.2 Hz, 1H; 10-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 13.95 (C-17), 14.35 (C-20), 17.91 (C-21), 61.28 (C-16), 61.95 (C-19), 125.26 (C-10), 126.52 (C-9), 127.06 (C-5), 127.55 (C-8), 128.03 (C-6), 128.40 (C-13), 128.78 (C-11), 129.06 (C-7), 129.53 (C-3), 130.45 (C-12), 132.29 (C-4), 132.34 (C-1), 133.76 (C-2), 134.04 (C-14), 167.42 (C-15), 172.11 ppm (C-18); **MS** (EI, 70 eV): *m/z* (%) = 337 (21) $[M+1]^+$, 336 (100) $[M^+]$, 227 (6) $[M–Et]^+$, 291 (42) $[C_{19}H_{15}O_3]^+$, 279 (18), 262 (42) $[C_{17}H_{10}O_3]^+$, 234 (22) $[C_{18}H_{15}O_2]^+$, 219 (14), 206 (7) $[C_{17}H_{15}O]^+$, 189 (26), 178 (8), 163 (6), 151 (2), 94 (9); **HRMS** (EI, M^+) calculated for $C_{21}H_{20}O_4$: 336.1361; found: 336.1369.

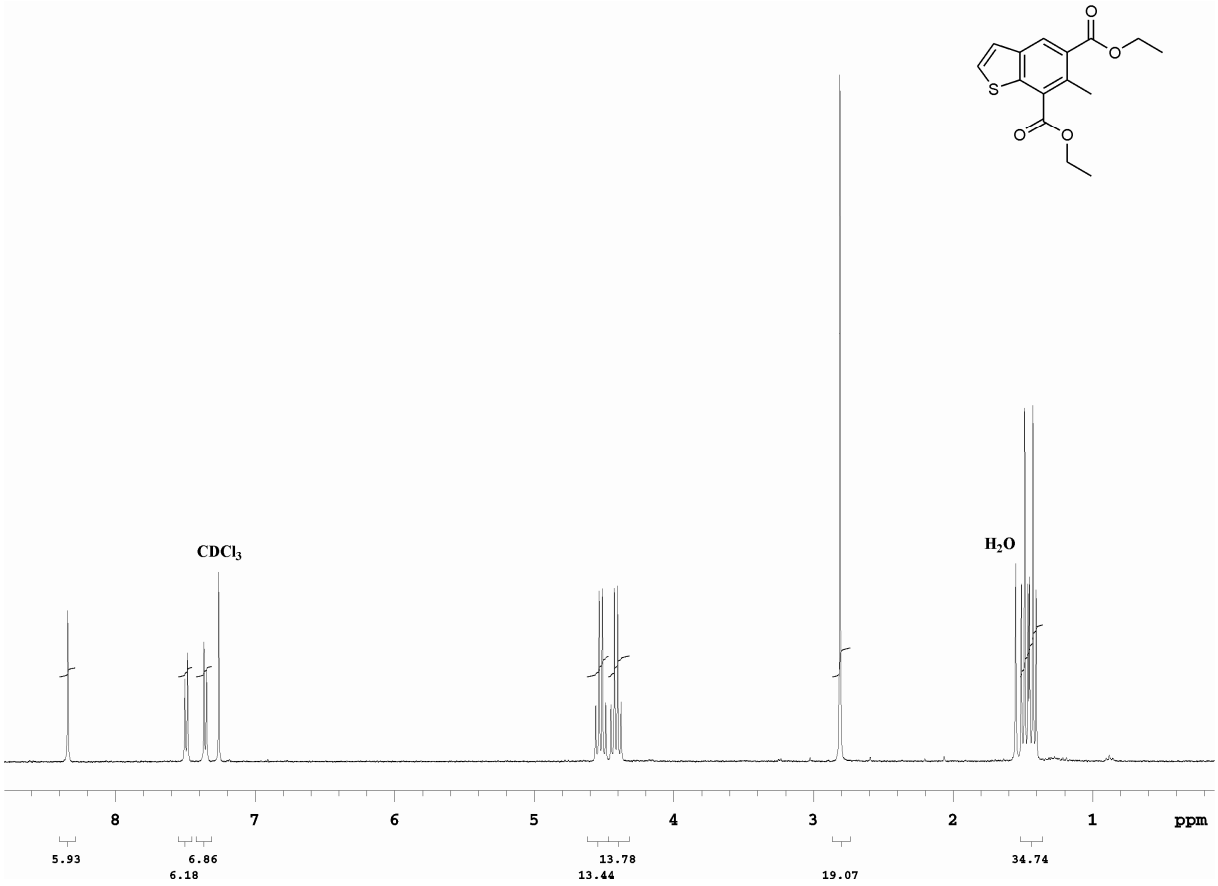
10. Synthesis of diethyl-6-methyl-benzo[*b*]thiophene-5,7-dicarboxylate (13)



13

An oven dried 10 mL vial was charged with 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%), 652 mg (2.0 mmol) Cs_2CO_3 (99.9%), 128 mg (0.5 mmol) 2-bromo-3-bromomethyl thiophene (**12**). The vial was sealed, evacuated and backfilled with argon (six times). 195 mg (1.5 mmol) freshly distilled ethyl acetoacetate (**2b**) and 3 mL of *N*-methyl pyrrolidine were added. The reaction mixture was heated in an oil bath at 80 °C for 24 h. After cooling to room temperature the reaction mixture was partitioned between 50 mL EtOAc and 20 mL brine. The aqueous phase was

extracted with EtOAc (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in *vacuo*. The residue thus obtained was purified by flash column chromatography over silica gel (cyclohexane/EtOAc = 20:1) to afford 115 mg (79%) diethyl-6-methyl-benzo[*b*]thiophene-5,7-dicarboxylate (**13**) as a colourless oil.



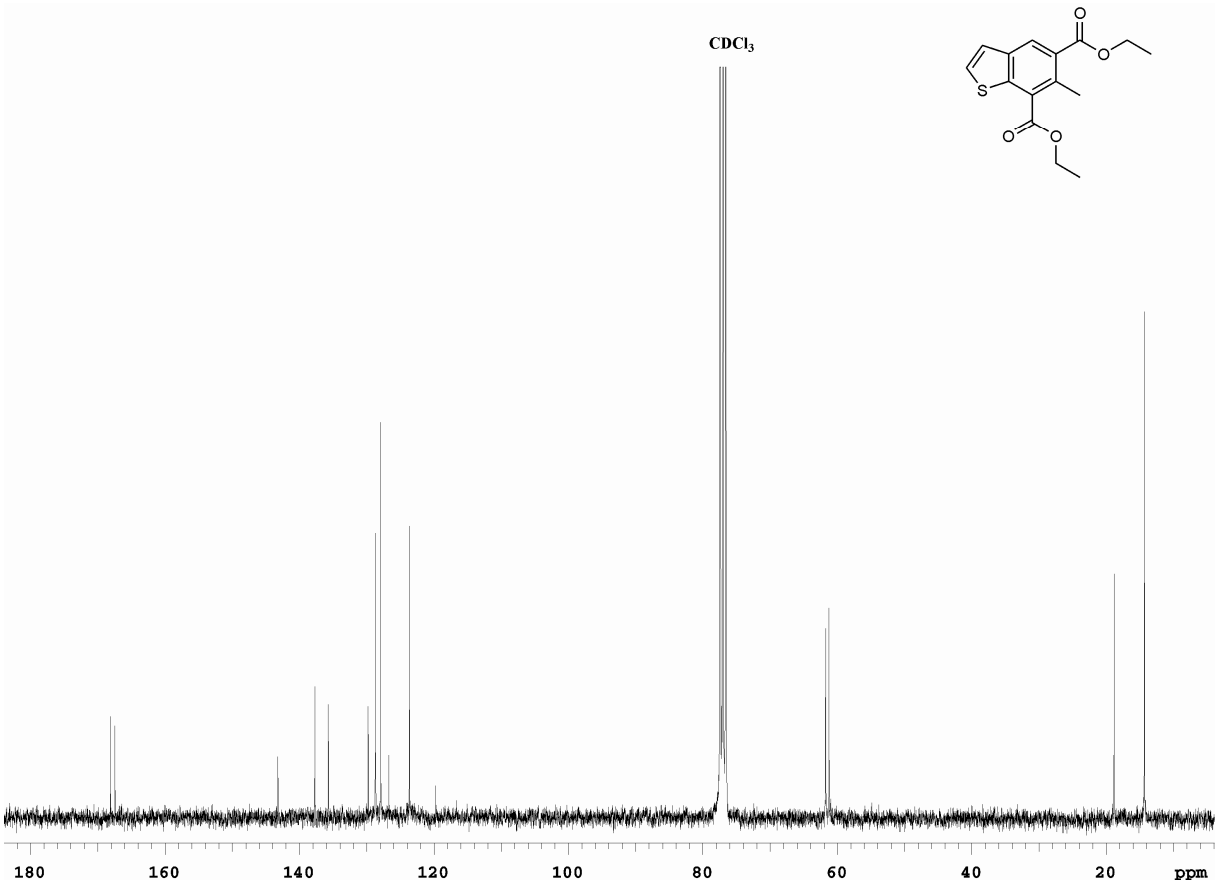
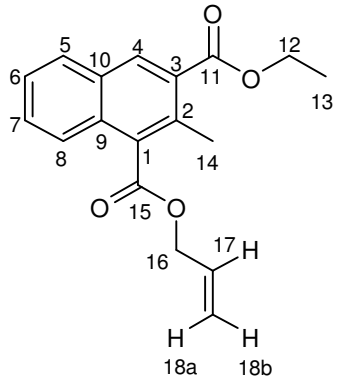


Figure 19. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **13** in $CDCl_3$.

$\boldsymbol{R_f}$ = 0.45 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2980 (w; CH_2, CH_3), 1711 (s; C=O), 1698 (s; C=O), 1472 (w), 1382 (m; alkane C-H), 1339 (m; alkane C-H), 1281 (m; ester C-O), 1238 (s; ester C-O), 1199 (s; ester C-O), 1139 (m), 1052 (m), 945 (s; arom. C-H), 911 (m; arom. C-H), 776 (s; alkane C-H), 744 cm^{-1} (s; alkane C-H); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 214 (4.58), 247 nm (4.33); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.43 (t, ^{3}J (11-H, 12-H) = 7.3 Hz, 3H; 12-H_3), 1.49 (t, ^{3}J (14-H, 15-H) = 7.3 Hz, 3H; 15-H_3), 2.81 (s, 3H; 16-H_3), 4.41 (q, ^{3}J (11-H, 12-H) = 7.4 Hz, 2H; 11-H_2), 4.53 (q, ^{3}J (14-H, 15-H) = 7.2 Hz, 2H; 14-H_2), 7.36 (d, ^{3}J (2-H, 3-H) = 5.7 Hz, 1H; 3-H), 7.49 (d, ^{3}J (2-H, 3-H) = 5.5 Hz, 1H; 2-H), 8.34 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.31 (C-12 and C-15), 18.83 (C-16), 61.24 (C-11), 61.72 (C-14), 123.63 (C-3), 126.71 (C-7), 127.92 (C-4), 128.70 (C-2), 129.77 (C-5), 135.74 (C-6), 137.70 (C-9), 143.19 (C-8), 167.43 (C-10), 168.13 ppm (C-13); **MS** (EI, 70 eV): *m/z* (%) = 293 (12) $[M+1]^+$, 292 (80) $[M^+]$, 263 (16) $[M–Et]^+$, 247 (58) $[C_{13}H_{11}SO_3]^+$, 235 (68) $[C_{12}H_{11}SO_3]^+$, 218 (100) $[C_{11}H_6SO_3]^+$, 190 (45) $[C_{10}H_6SO_2]^+$, 145 (23), 91 (19) $[C_7H_7]^+$; **HRMS** (EI, M^+) calculated for $C_{15}H_{16}SO_4$: 292.0770; found: 292.0768.

11. Synthesis of allyl-ethyl-2-methylnaphthalene-1,3-dicarboxylate (9j)



9j

An oven dried 10 mL vial was charged with 9.5 mg (0.05 mmol) CuI (99.999%), 18.6 mg (0.15 mmol) picolinic acid (**8**) (99%), 652 mg (2.0 mmol) Cs_2CO_3 (99.9%) and 150 mg (0.5 mmol) 2-acetyl-3-(2-bromophenyl)propionate (**7**). The vial was sealed, evacuated and backfilled with argon (six times). Then 107 mg (0.75 mmol) freshly distilled allyl acetoacetate (**2e**) and 3 mL *N*-methyl pyrrolidine were added. The reaction mixture was heated in an oil bath at 100 °C for 24 h. After cooling to room temperature the reaction mixture was partitioned between 50 mL EtOAc and 20 mL brine. The aqueous phase was extracted with EtOAc (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in *vacuo*. The residue thus obtained was purified by flash column chromatography over silica gel (cyclohexane/EtOAc = 20:1) to afford 91 mg (61%) allyl-ethyl-2-methylnaphthalene-1,3-dicarboxylate (**9j**) as a colourless oil. In addition, 5% of **3b** were isolated.

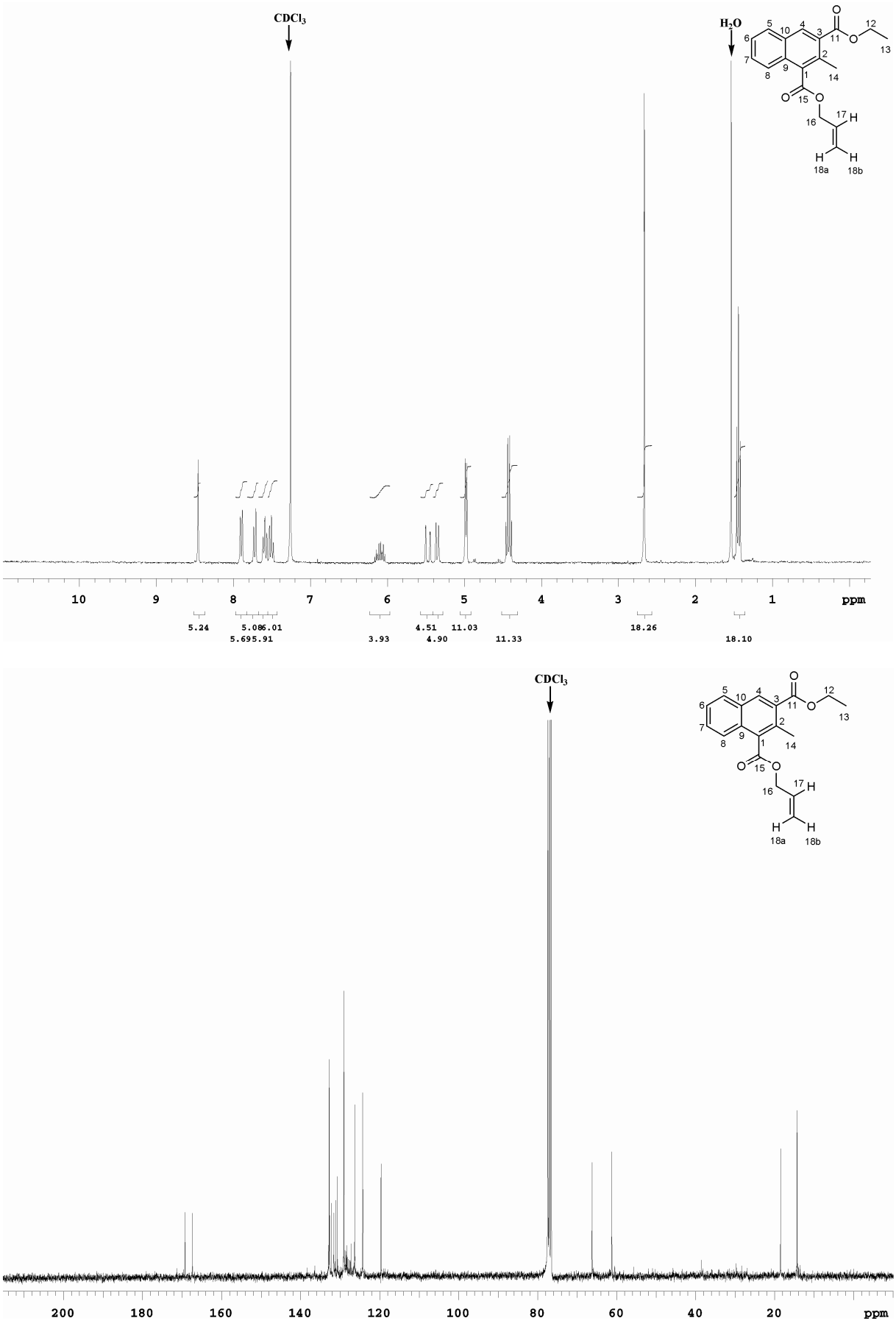


Figure 20. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra of **9j** in $CDCl_3$.

$\boldsymbol{R_f}$ = 0.48 (cyclohexane/EtOAc = 5:1); **IR** (ATR): $\tilde{\nu}$ = 2950 (w; CH_2, CH_3), 1712 (s; C=O), 1487 (m), 1438 (m), 1375 (w; alkane C-H), 1276 (m; ester C-O), 1243 (s; ester C-O), 1237 (s; ester C-O), 1046 (m), 1067 (m), 1045 (m), 991 (s), 928 (s; arom. C-H), 917 (s; arom. C-H) (s), 783 (s), 752 (s; alkane C-H) (s), 728 cm^{-1} (m); **UV/Vis** (CH_3CN): λ_{max} (log ε) = 230 (4.45), 234 (4.46), 238 (4.45), 282 nm (3.58); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.44 (t, ^3J (12-H, 13-H) = 7.2 Hz, 3H; 13-H_3), 2.67 (s, 3H; 14-H_3), 4.43 (q, ^3J (12-H, 13-H) = 7.2 Hz, 2H; 12-H_2), 4.98 (ddd, ^2J (16-H, 16-H) = 1.6 Hz, ^3J (16-H, 17-H) = 6.0 Hz, ^4J (16-H, 18-H) = 1.2 Hz, 2H; 16-H_2), 5.35 (ddt, ^2J (18a-H, 18b-H) = 1.4 Hz, $^3J_{cis}$ (17-H, 18b-H) = 10.7 Hz, ^4J (16-H, 18b-H) = 1.2 Hz, 1H; 18b-H), 5.48 (ddt, ^2J (18a-H, 18b-H) = 1.4 Hz, $^3J_{trans}$ (17-H, 18a-H) = 17.2 Hz, ^4J (16-H, 18a-H) = 1.4 Hz, 1H; 18a-H), 6.11 (m, 1H; 17-H), 7.52 (ddd, ^3J (6-H, 7-H) = 6.9 Hz, ^3J (5-H, 6-H) = 7.7 Hz, ^4J (6-H, 8-H) = 1.3 Hz, 1H; 6-H), 7.59 (ddd, ^3J (6-H, 7-H) = 6.9 Hz, ^3J (7-H, 8-H) = 8.4 Hz, ^4J (5-H, 7-H) = 1.5 Hz, 1H; 7-H), 7.72 (br d, ^3J (7-H, 8-H) = 8.1 Hz, 1H; 8-H), 7.90 (br d, ^3J (5-H, 6-H) = 8.1 Hz, 1H; 5-H), 8.46 (s, 1H; 4-H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 14.33 (C-13), 18.52 (C-14), 61.21 (C-12), 66.19 (C-16), 119.62 (C-18), 124.29 (C-8), 126.31 (C-6), 128.34 (C-3), 128.98 (C-5), 129.05 (C-7), 130.68 (C-10), 131.13 (C-9), 131.57 (C-17), 132.23 (C-2), 132.64 (C-1), 132.75 (C-4), 167.37 (C-11), 169.26 ppm (C-15); **MS** (EI, 70 eV): *m/z* (%) = 300 (4) $[M+2]^+$, 299 (7) $[M+1]^+$, 298 (29) $[M^+]$, 270 (8) $[M–CO]^+$, 253 (18) $[C_{16}H_{13}O_3]^+$, 241 (32) $[C_{15}H_{13}O_3]^+$, 229 (100), 211 (65) $[C_{14}H_{11}O_2]^+$, 169 (16), 139 (53) $[C_{11}H_7]^+$, 128 (23); **HRMS** (EI, M^+) calculated for $C_{18}H_{18}O_4$: 298.1205; found: 298.1221.

12. References

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