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PREPARATION OF DIETHYL MALONATE ADDUCTS FROM CHALCONE ANALOGS CONTAINING A THIENYL RING

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ABSTRACT. Nine chalcone-diethyl malonate derivatives (**4a-i**) were prepared by the reaction of chalcone derivatives (**3a-i**) with diethyl malonate in the presence of a catalytic amount of KO*t*-Bu in CH_2CI_2 in good to excellent yields. The products were characterized by FTIR, ^{1}H-NMR, ^{13}C-NMR and elemental analyses.

KEY WORDS: Michael addition, Chalcone, KO*t*-Bu, Diethyl malonate

INTRODUCTION

Chalcone and its derivatives are medicinally important. Many chalcone derivatives have been reported to possess antimalarial, antibacterial, and antifungal properties [1-3]. Anticancer properties of some simple chalcone derivatives have been reported in the literature [4]. Chalcones are also important compounds as Michael acceptors in organic synthesis [5-9]. Michael addition reaction of appropriate carboanionic reagents to α,β-unsaturated carbonyl compounds such as chalcones is of synthetic interest for C-C bond formation [10]. Addition of 1,3-dicarbonyl compounds such as malonate esters and acetoacetate esters is important for synthesis of 1,5-dicarbonyl compounds which are the key compounds for the preparation of many biological heterocyclic compounds [11]. Many studies have been reported on related addition of diethyl malonate to chalcone derivatives [12-13].

Addition, methylenecarboxy groups are key functionalities in many biologically active compounds such as the antiinflammatory and analgesic drugs indomethacin or aclofenac [14]. A mild and efficient procedure for the introduction of the methylenecarboxy group into functionalized molecules is thus of great interest.

In this study, novel chalcone-diethyl malonate derivatives that can be used in the synthesis of acid derivatives were synthesized from the chalcone analog containing thienyl ring.

RESULTS AND DISCUSSION

A series of 9 chalcone-diethyl malonate derivatives (**4a-i**) was prepared by addition of diethyl malonate to chalcones (**3a-i**) (Scheme 1). To a solution of chalcone and diethyl malonate in CH_2Cl_2 at room temperature was added a catalytic amount of KO*t*-Bu and continued to stirred for 3-4 h. After removing the solvent, the residue was purified on a silica gel column eluting with CH_2Cl_2/*n*-hexane (3:2). After purification of the residue, diethyl malonate adducts (**4a-i**) were obtained in yields of 72–94%. The results are summarized in Table 1. The structures of all the 9 adducts of diethyl malonate (**4a-i)** synthesized in this study were established on the basis of IR, ^{1}H-, ^{13}C-NMR, elemental analysis data and comparison with similar results in the literature [15, 16]. The addition of diethyl malonate to chalcones **3a-i** leads to the generation of two chiral centers in the structure of adducts **4a-i**. The carbon atoms of ethoxy groups show diastereotopic properties due to the two chiral centers. For this reason, in the ^{1}H-NMR spectra

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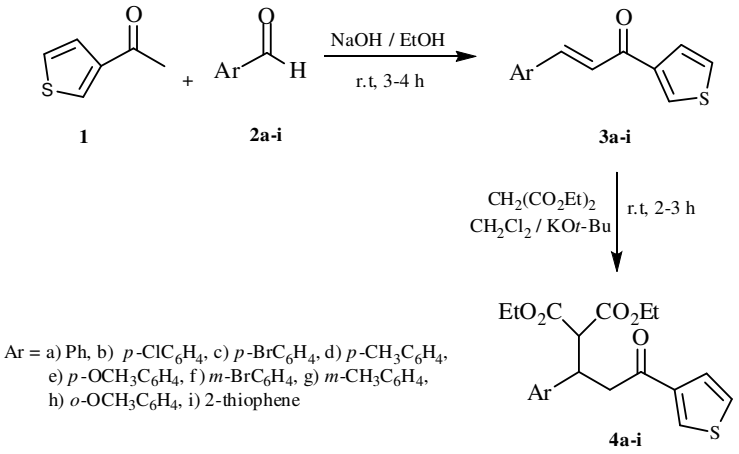
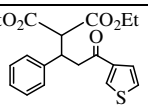
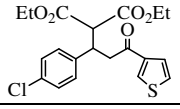
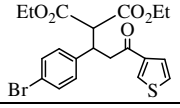
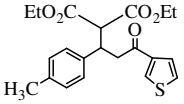
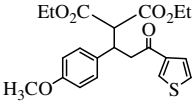
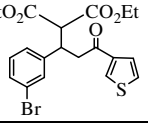
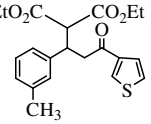
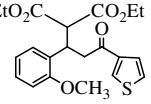
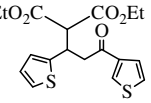
of **4a-i**, methyl groups give two signals at about 14 and 13 ppm, and there are smiliar results in the literature [17]. Additional structural analysis of the newly synthesized diethyl malonate adducts **4a-i** comprised IR investigations. The IR spectra of these compounds revealed two sharp strong absorption bands around 1732-1771 ($\nu_{c=o}$ ester) cm^{-1} [13]. The results are in agreement with the proposed structures. The compounds **4a-i** are new according to our literature survey.



Scheme 1

Table 1. Synthesized compounds **4a**-**i**.

Entry	Compound No.	Products	M.p. (^{0}C)	Yield (%)
1	**4a**		105-106	94
2	**4b**		132-134	91
3	**4c**		83-85	90
4	**4d**		129-131	75
5	**4e**		62-64	77

6	**4f**		107-108	73
7	**4g**		95-97	86
8	**4h**		75-77	92
9	**4i**		89-91	72

Consequently, 9 chalcone-diethyl malonate derivatives (**4a-i**) were prepared in high yields under mild reaction conditions. Under the optimized reaction conditions, various substituted chalcones acting as Michael acceptors were allowed to react with malonate and the results are summarized in Table 1. Compounds **4a**–**i** are colourless materials, which are stable, sparingly soluble in hydrocarbons and readily soluble in chloroform, alcohols and dimethyl sulfoxide.

EXPERIMENTAL

General

1-(Thien-3-yl)ethanone (**1**) and the aldehyde derivatives **2a-i** are commercially available (Merck). All solvents were dried and distilled with standard procedures. Melting points were measured on an Electrothermal 9100 apparatus (Tokat, Turkey) and are uncorrected. IR spectra (KBr or liquid) were recorded on a Jasco FT/IR-430 spectrometer (Tokat, Turkey). ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance III 400 instrument (Tokat Turkey). As internal standards served TMS (δ 0.00) for ^{1}H NMR, and $CDCl_3$ (δ 77.0) for ^{13}C NMR. The coupling constant *J* values are given in Hz. The multiplicities of the signals in the ^{1}H NMR spectra are abbreviated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) and combinations thereof. Elemental analyses were obtained from a Leco CHNS 932 Elemental analyzer (Malatya, Turkey).

*General procedure for syntheses of chalcones **3a-i***

To a solution of 1-(thiophen-3-yl)ethanone (**1**) (0.5 g, 4 mmol) and benzaldehyde derivatives **2a-i** (4 mmol) in EtOH (15 mL), an aqueous solution of sodium hydroxide (NaOH) (5%, 5 mL) was added. The temperature was kept at ca. 25 ^{o}C, and the mixture was stirred vigorously for 3-4 h. Then, it was neutralized with dilute HCl. The mixture was extracted with $CHCl_3$ (3 x 10 mL). The combined organic extracts were washed with water (50 mL) and dried (Na_2SO_4). The solvent was evaporated (45 ^{o}C, 20 mmHg), purified by crystallization from a mixture of *n*-hexane and CH_2Cl_2 (5:1).

*3-Phenyl-1-(thiophen-3-yl)prop-2-en-1-one (**3a**)*. Yield: 98%; colorless crystals; m.p. 105-106 ^{o}C. IR ν (KBr): 3094, 2961, 2840, 1670, 1638, 1617, 1515, 1417, 1229, 1192, 976, 762, 618

cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.19 (m, 1H), 7.83 (d, *J* = 16 Hz, 1H) 7.69 (br d, *J* = 5 Hz, 1H), 7.65-7.63 (m, 2H), 7.44-7.40 (m, 4H), 7.37 (dd, *J* = 5, 2.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.93, 144.09, 143.10, 134.80, 132.16, 130.55, 128.98, 128.46, 127.47, 126.56, 122.69. Anal. calc. for $C_{13}H_{10}OS$**:** C, 72.87; H, 4.70; S, 14.96. Found: C, 72.60; H, 4.42; S, 15.14.

*3-(4-Chlorophenyl)-1-(thiophen-3-yl)prop-2-en-1-one (**3b**)*.Yield: 98%; yellowish crystals; m.p. 124-125 °C. IR ν (KBr): 3084, 1615, 1564, 1405, 1229, 1197, 1087, 861, 758, 602 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.17 (m, 1H), 7.76 (d, *J* = 16 Hz, 1H), 7.67 (dd, *J* = 5, 0.8 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.40-7.36 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.60, 142.95, 142.85, 136.38, 133.28, 132.25, 129.58 (2C), 129.24 (2C), 127.41, 126.64, 123.07; Anal. calc. for $C_{13}H_9ClOS$**:** C, 62.78; H, 3.65; S, 12.89. Found: C, 62.57; H, 3.63; S, 12.59.

*3-(4-Bromophenyl)-1-(thiophen-3-yl)prop-2-en-1-one (**3c**)*. Yield: 98%; colorless crystals; m.p. 132-133 °C. IR ν (KBr): 3084, 2963, 2846, 1617, 1561, 1484, 1229, 1192, 976, 762, 618 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.17 (m, 1H), 7.74 (d, *J* = 15.6 Hz, 1H), 7.65-7.63 (m, 1H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.41-7.36 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.58, 142.93, 142.63, 133.71, 132.26, 132.19 (2C), 129.77 (2C), 127.41, 126.64, 124.76, 123.18. Anal. calc. for $C_{13}H_9BrOS$: C, 53.26; H, 3.09; S, 10.94. Found: C, 53.02; H, 3.13; S, 10.96.

*1-(Thiophen-3-yl)-3-p-tolylprop-2-en-1-one (**3d**)*. Yield: 99%; colorless crystals; m.p. 118-119 °C. IR ν (KBr): 3103, 2968, 2842, 1638, 1509, 1229, 1180, 1026, 992, 798, 622 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.17- 8.16 (m, 1H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.69-7.67 (m, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.23-7.21 (m, 2H), 2.39 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 184.03, 144.17, 143.21, 141.06, 132.07, 131.93, 129.72, 128.47, 127.48, 126.44, 121.71, 21.55. Anal. calc. for $C_{14}H_{12}OS$**:** C, 73.65; H, 5.30; S, 14.04. Found: C, 73.38; H, 5.13; S, 13.87.

*3-(4-Methoxyphenyl)-1-(-3-yl)prop-2-en-1-one (**3e**)*. Yield: 98%; yellowish crystals; m.p. 47-48 °C. IR ν (KBr): 3091, 3001, 2960, 2836, 1654, 1462, 1440, 1353, 1316 1225, 1183, 1072, 806, 728, 625 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.17-8.15 (m, 1H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.67 (dd, *J* = 5, 0.9 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.37-7.35 (m, 1H), 7.31 (d, *J* = 15.6 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 2H), 3.85 (s, 3H, -OCH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 184.02, 161.65, 143.94, 143.30, 131.73, 130.21(2C), 127.51, 127.41, 126.39, 120.38, 114.42 (2C), 55.41. Anal. calc. for $C_{14}H_{12}O_2S$**:** C, 68.83; H, 4.95; S, 13.12. Found: C, 68.61; H, 4.73; S, 13.39.

*3-(3-Bromophenyl)-1-(thiophen-3-yl)prop-2-en-1-one (**3f**)*. Yield: 97%; colorless crystals; m.p. 91-92 °C. IR ν (KBr): 3105, 2970, 2849, 1656, 1600, 1505, 1402, 1300, 1226, 1179, 781, 669, 575 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.19-8.18 (m, 1H), 7.76 (br s, 1H), 7.70 (d, *J* = 15.6 Hz, 1H), 7.67 (d, *J* = 5.1 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.40-7.35 (m, 2H), 7,27 (t, *J* = 7.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.39, 142.86, 142.18, 136.92, 133.19, 132.45, 130.78, 130.46, 127.42, 127.25, 126.68, 123.89, 123.08. Anal. calc. for $C_{13}H_9BrOS$: C, 53.26; H, 3.09; S, 10.94. Found: C, 52.98; H, 3.21; S, 11.06.

*1-(Thiophen-3-yl)-3-m-tolylprop-2-en-1-one (**3g**)*. Yield: 99%; yellowish crystals; m.p. 80-81 °C. IR ν (KBr): 3084, 2968, 2842, 1638, 1616, 1598, 1510, 1412, 1242, 1198, 1033, 984, 782, 714, 681 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.19-8.18 (m, 1H), 7.81 (d, *J* = 15.6 Hz, 1H), 7.69 (dd, *J* = 5, 0.9 Hz, 1H), 7.45-7.43 (m, 3H), 7.39-7.36 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 1H),

7.23 (t, *J* = 7.4 Hz, 1H), 2.40 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.97, 144.30, 143.15, 138.62, 134.76, 132.04, 131.40, 129.05, 128.86, 127.48, 126.48, 126.69, 122.51, 21.86. Anal. calc. for $C_{14}H_{12}OS$**:** C, 73.65; H, 5.30; S, 14.04. Found: C, 73.34; H, 5.17; S, 14.33.

*3-(2-Methoxyphenyl)-1-(thiophen-3-yl)prop-2-en-1-one (**3h**)*. Yield: 93%; colorless crystals; m.p. 69-70 °C. IR ν (KBr): 3092, 2961, 2845, 1617, 1509, 1414, 1322, 1248, 1186, 1032, 989, 862, 816, 751 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.16-8.15 (m, 1H), 7.67-7.66 (br d, *J* = 5 Hz, 1H), 7.62 (br d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 15 Hz, 1H), 7.38-7.33 (m, 3H), 6.98 (t, *J* = 8 Hz, 1H), 6.92 (d, *J* = 8 Hz, 1H), 3.88 (s, 3H, -OCH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 184.54, 164.03, 158.78, 143.34, 139.60, 131.91, 131.77, 129.20, 127.54, 126.35, 123.80, 123.80, 123.50, 120.75, 111.26. Anal. calc. for $C_{14}H_{12}O_2S$**:** C, 68.83; H, 4.95; S, 13.12. Found: C, 68.67; H, 4.69; S, 13.41.

*3-(Thiophen-2-yl)-1-(thiophen-3-yl)prop-2-en-1-one (**3i**)*. Yield: 96%; yellowish crystals; m.p. 82-83 °C. IR ν (KBr): 3100, 3088, 2975, 2849, 1640, 1616, 1602, 1572, 1508, 1499, 1409, 1313, 1225, 1183, 1020, 806, 728, 702, 635 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.15 (m, 1H), 7.94 (d, *J* = 15.6 Hz, 1H), 7.67 (br d, *J* = 5 Hz, 1H), 7.43 (d, *J* = 3.9 Hz, 1H), 7.38-7.34 (m, 2H), 7.21 (d, *J* = 15.6 Hz, 1H), 7.11-7.07 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.38, 143.02, 140.27, 136.49, 132.03, 131.97, 128.73, 128.36, 127.40, 126.50, 121.49. Anal. calc. for $C_{11}H_8OS_2$: C, 59.97; H, 3.66; S, 29.11. Found: C, 59.71; H, 3.57; S, 29.41.

*General procedure for addition of diethylmalonate to chalcone derivatives **3a-i***

A solution of chalcone derivatives **3a-i** (1 mmol) and diethyl malonate (1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 2-3 h in the presence of a catalytic amount of KO*t*-Bu. The reaction mixture was extracted with CH_2Cl_2 and the organic layer was washed with H_2O, and dried (Na_2SO_4). The solvent was evaporated (45 °C, 20 mmHg). The crude product was filtrated on a silica gel column, and crystallized from CH_2Cl_2 and *n*-hexane (5:1), (**4a-i** yields, 72–94%).

*Diethyl 2-(3-oxo-1-phenyl-3-(thiophen-3-yl)propyl)malonate (**4a**)*. Yield: 94%; colorless crystals; m.p. 105-106 °C. IR ν (KBr): 3094, 2964, 2925, 1754, 1736, 1637 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.17-8.16 (m, 1H), 7.71-7.66 (m, 1H), 7.64-7.63 (m, 1H), 7.54-7.1 (m, 2H), 7.43-7.39 (m, 2H), 7.38 (m, 1H); 4.25-4.21 (m, 3H); 3.93 (q, *J* = 7.0 Hz, 2H), 3.79 (d, *J* = 9.3 Hz, 1H), 3.49 (dd, *J* = 15.7, 4.3 Hz, 1H), 3.41 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.09 (t, *J* = 7.0 Hz, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 189.21, 167.51, 167.31, 144.90, 143.94, 133.67 (2C), 130.50 (2C), 128.53, 127.36 (2C), 125.11, 63.12, 61.71, 57.03, 42.01, 40.63, 14.15, 13.92. Anal. calc. for $C_{20}H_{22}O_5S$**:** C, 64.15; H, 5.92; S, 8.56. Found: C, 64.22; H, 5.99; S, 8.48.

*Diethyl 2-(1-(4-chlorophenyl)-3-oxo-3-(thiophen-3-yl)propyl)malonate (**4b**)*. Yield: 91%; colorless crystals; m.p. 132-134 °C. IR ν (KBr): 3099, 2954, 1765, 1742, 1675 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.17 (m, 1H), 7.69 (d, *J* = 5.2 Hz, 1H), 7.54 (dd, *J* = 6.8, 1.2 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.28-7.24 (m, 2H), 4.23-4.18 (m, 2H), 4.12-4.11 (m, 1H), 3.85 (q, *J* = 6.9 Hz, 2H), 3.72 (d, *J* = 9.5 Hz, 1H), 3.49 (dd, *J* = 15.6, 4.2 Hz, 1H), 3.36 (dd, *J* = 15.6, 9.3 Hz, 1H), 1.27 (t, *J* = 6.9 Hz, 3H), 1.14 (t, *J* = 6.9 Hz, 3H), ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 188.42, 169.81, 167.44, 142.90, 140.54, 132.17 132.04 (2C), 130.80 (2C), 128.28, 127.96, 127.96 (2C), 122.87, 67.87, 66.31, 59.38, 44.86, 38.53, 14.33, 13.97. Anal. calc. for $C_{20}H_{21}ClO_5S$**:** C, 58.75; H, 5.18; S, 7.84. Found: C, 58.83; H, 5.26; S, 7.96.

*Diethyl 2-(1-(4-bromophenyl)-3-oxo-3-(thiophen-3-yl)propyl)malonate (**4c**)*. Yield: 90%; colorless crystals; m.p. 83-85 °C. IR ν (KBr): 3087, 2960, 2925, 1755, 1739, 1637 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.09-8.08 (m, 1H), 7.49 (d, *J* = 4.8 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.28-7.27 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 4.27-4.19 (m, 2H), 4.13-4.08 (m, 1H), 3.98 (q, *J* = 7.0 Hz, 2H), 3.77 (d, *J* = 9.6 Hz, 1H), 3.44 (dd, *J* = 15.9, 4.0 Hz, 1H), 3.29 (dd, *J* = 15.9, 9.6 Hz, 1H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 191.50, 168.11, 167.50, 141.86, 139.36, 132.28 131.51 (2C), 130.02 (2C), 127.40, 126.87 (2C), 121.09, 61.79, 61.51, 57.17, 43.63, 40.41, 14.11, 13.78. Anal. calc. for $C_{20}H_{21}BrO_5S$**:** C, 52.99; H, 4.67; S, 7.07. Found: C, 53.09; H, 4.59; S, 7.17.

*Diethyl 2-(3-oxo-3-(thiophen-3-yl)-1-p-tolylpropyl)malonate (**4d**)*. Yield: 75%; colorless crystals; m.p. 129-131 °C. IR ν (KBr): 3110, 3087, 2935, 2935, 1735, 1731, 1643 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.12- 8.11 (m, 1H), 7.71 (d, *J* = 15.5 Hz, 1H), 7.61-7.58 (m, 1H), 7.54-7.55 (m, 2H), 7.46-7.42 (m, 2H), 4.21-4.10 (m, 3H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.80 (d, *J* = 9.5 Hz, 1H), 3.41 (dd, *J* = 17.4, 4.5 Hz, 1H), 3.25 (dd, *J* = 17.4, 9.2 Hz, 1H), 2.34 (s, 3H); 1.21 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 185.10, 168.11, 167.50, 143.23, 142.14, 140.21, 132.36, 131.13, 128.87, 128.12, 127.15, 61.12, 60.87, 56.81, 44.52, 41.34, 21.52, 14.08, 13.97. Anal. calc. for $C_{21}H_{24}O_5S$**:** C, 64.93; H, 6.23; S, 8.25. Found: C, 64.81; H, 6.36; S, 8.12.

*Diethyl 2-(1-(4-methoxyphenyl)-3-oxo-3-(thiophen-3-yl)propyl)malonate (**4e**)*. Yield: 77%; colorless crystals; m.p. 62-64 °C. IR ν (KBr): 3081, 2960, 2925, 1749, 1734, 1637 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.16-8.14 (m, 1H), 7.85 (d, *J* = 15.6 Hz, 1H), 7.69 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.61-7.59 (m, 1H), 7.37-7.34 (m, 1H), 7.27-7.21(m, 1H), 6.94-6.92 (m, 1H), 4.24-4.18 (m, 3H), 3.89 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.79 (d, *J* = 9.5 Hz, 1H), 3.69 (dd, *J* = 17.4, 4.5 Hz, 1H), 3.36 (dd, *J* = 17.4, 9.2 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 190.79, 167.88, 167.74, 143.91, 143.31, 131.66, 130.18 (2C), 128.78, 127.53, 127.46, 126.96 (2C), 61.48, 60.13, 57.69, 55.39, 47.47, 41.66, 14.04, 13.67. Anal. calc. for $C_{21}H_{24}O_6S$**:** C, 62.36; H, 5.98; S, 7.93. Found: C, 62.45; H, 6.12; S, 7.82.

*Diethyl 2-(1-(3-bromophenyl)-3-oxo-3-(thiophen-3-yl)propyl)malonate (**4f**)*. Yield: 73%; colorless crystals; m.p. 107-108 °C. IR ν (KBr): 3115, 3075, 2954, 1765, 1745, 1643 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.15-8.12 (m, 1H), 7.73 (d, *J* = 15.6 Hz, 1H), 7.67-7.63 (m, 1H), 7.56-7.52 (m, 2H), 7.44-7.37 (m, 2H), 4.27-4.15 (m, 3H), 3.98 (q, *J* = 6.9 Hz, 2H), 3.83 (d, *J* = 9.5 Hz, 1H), 3.48 (dd, *J* = 15.8, 4.2 Hz, 1H), 3.37 (dd, *J* = 15.8, 9.5 Hz, 1H), 1.25 (t, *J* = 6.9 Hz, 3H), 1.00 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.94, 168.38, 166.63, 144.10, 143.10, 136.85, 133.21, 132.06, 130.52 128.96, 128.42, 127.47, 126.23, 68.15, 61.69, 57.50, 38.73, 33.39, 14.06, 13.74. Anal. calc. for $C_{20}H_{21}BrO_5S$: C, 52.99; H, 4.67; S, 7.07. Found: C, 52.91; H, 4.73; S, 7.01.

*Diethyl 2-(3-oxo-3-(thiophen-3-yl)-1-m-tolylpropyl)malonate (**4g**)*. Yield: 86%; colorless crystals; m.p. 95-97 °C. IR ν (KBr): 3091, 2961, 1760, 1743, 1650 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18-8.17 (m, 1H), 7.80 (d, *J* = 15.4 Hz, 1H), 7.54-7.51 (m, 1H), 7.44-7.41 (m, 2H), 7.38-7.35 (m, 2H); 4.25-4.17 (m, 3H), 3.95 (q, *J* = 7.0 Hz, 2H), 3.76 (d, *J* = 9.5 Hz, 1H), 3.49 (dd, *J* = 15.7, 4.2 Hz, 1H), 3.33 (dd, *J* = 15.7, 9.5 Hz, 1H), 2.40 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 0. 94 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.93, 167.72, 166.60, 144.26, 138.58, 134.75 132.03, 131.36, 130.87, 129.01, 128.82, 127.45, 125.67, 68.11, 61.46, 60.65, 38.71, 28.90, 21.31, 14.03, 13.94. Anal. calc. for $C_{21}H_{24}O_5S$: C, 64.93; H, 6.23; S, 8.25. Found: C, 64.99; H, 6.32; S, 8.19.

*Diethyl 2-(1-(2-methoxyphenyl)-3-oxo-3-(thiophen-3-yl)propyl)malonate (**4h**)*. Yield: 92%; colorless crystals; m.p. 75-77 °C. IR ν (KBr): 3099, 2952, 1768, 1755, 1660 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.15-8.14 (m, 1H), 7.72-7.69 (br d, *J* = 4.3 Hz, 1H), 7.67 (br d, *J* = 6.4 Hz, 1H), 7.54-7.50 (m, 2H), 7.39-7.35 (m, 2H), 4.21-4.13 (m, 3H), 3.93 (q, *J* = 6.9 Hz, 2H), 3.81 (d, *J* = 9.5 Hz, 1H), 3.53 (dd, *J* = 16.2, 4.2 Hz, 1H), 3.41 (dd, *J* = 16.2, 9.5 Hz, 1H), 3.36 (s, 3H), 1.28 (t, *J* = 6.9 Hz, 3H), 1. 12 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 188.10, 167.73, 156.97, 143.33, 139.64, 131.80, 131.69, 129.23, 128.78, 127.54, 126.27, 123.57, 120.72, 68.19, 61.71, 60.83, 55.19, 42.71, 40.90, 14.11, 13.96. Anal. calc. for $C_{21}H_{24}O_6S$: C, 62.36; H, 5.98; S, 7.93. Found: C, 62.45; H, 6.03; S, 8.09.

*Diethyl 2-(3-oxo-1-(thiophen-2-yl)-3-(thiophen-3-yl)propyl)malonate (**4i**)*. Yield: 72%; colorless crystals; m.p. 89-91 °C. IR ν (KBr): 3096, 3072, 1771, 1732, 1649 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.10-8.09 (m, 1H), 7.86-7.82 (m, 1H), 7.63-7.61 (m, 1H), 7.46-7.41 (m, 1H), 7.34-7.32 (m, 2H), 4.13-4.18 (m, 2H); 4.00-3.98 (m, 1H); 3.95 (q, *J* = 6.9 Hz, 2H), 3.72 (d, *J* = 9.5 Hz, 1H), 3.44 (dd, *J* = 15.9, 4.2 Hz, 1H), 3.37 (dd, *J* = 15.9, 9.3 Hz, 1H), 1.24 (t, *J* = 6.9 Hz, 3H), 1.02 (t, *J* = 6.9 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 183.14, 167.89, 166.47, 142.94, 140.16, 136.26, 132.25, 131.88, 128.27, 127.27, 121.41, 67.95, 66.89, 57.70, 44.91, 38.64, 14.10, 13.92. Anal. calc. for $C_{18}H_{20}O_5S_2$: C, 56.82; H, 5.30; S, 16.86. Found: C, 56.71; H, 5.41; S, 16.93.

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