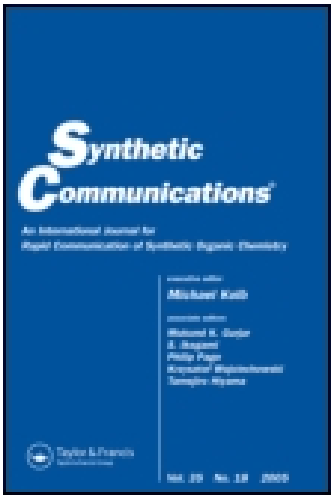

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Potassium-Tertiary Butoxide-Assisted Addition of Thioglicolic Acid to Chalcone Derivatives Under Solvent-Free Conditions

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POTASSIUM–TERTIARY BUTOXIDE–ASSISTED ADDITION OF THIOGLICOLIC ACID TO CHALCONE DERIVATIVES UNDER SOLVENT-FREE CONDITIONS

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A series of chalcone derivatives containing thioglicolic acid (4a–j) was prepared by addition of thioglicolic acid to the chalcones (3a–j) in the presence of KOt-Bu under solvent-free conditions. The mechanistic pathway of the reaction can be explained by the Michael-type addition of thioglicolic acid to chalcone derivatives (3a–j).

Keywords: Michael addition; potassium–tertiary butoxide; solvent free; thioglicolic acid

Carbon–sulfur bond formation by conjugate addition of thiols to α,β-unsaturated carbonyl compounds has versatile applications in chemistry and biology as it plays critical roles in (i) biosynthesis,[1] (ii) synthesis of bioactive compounds,[2] (iii) protection of the olefinic double bond of conjugated enones,[3] and (iv) generation of β-acylvinyl cation[4] and homoenolate anion[5] equivalents. Traditionally, the 1,4-addition of thiols is catalyzed by strong bases such as alkali metal alkoxides, hydroxides, and amines.[6,7] On the other hand, these reactions were also investigated using solid acids such as $HClO_4$–SiO_2[8] and different Lewis acids such as $InBr_3$,[9] $Zn(ClO_4)_2 \cdot 6H_2O$,[10] $Hf(OTf)_3$,[11] $Bi(NO3)_3$,[12] $Bi(OTf)_3$,[13] and $Cu(BF_4)_2$;[14] ionic liquid [pmIm]Br,[15,16] and organocatalyst in solvent-free conditions.[17] Most of the methods have some disadvantages such as long reaction times, high reaction temperatures, dry or stringent reaction conditions, complex workup procedures, and moderate yields. This study reports the addition of thioglicolic acid as thiol to chalcones in mild conditions in the presence of a small amount of potassium–tertiary butoxide. This reaction occurs without solvent in a short reaction time at room temperature and results in excellent yields.

The general synthetic strategy employed to prepare the chalcone derivatives was based on Claisen–Schmidt condensation, which was reported previously.[18] As shown in Scheme 1, a series of 11 chalcone derivatives (**3a–j**) was prepared upon condensation of appropriately substituted acetophenone with furfural in EtOH (Scheme 1).

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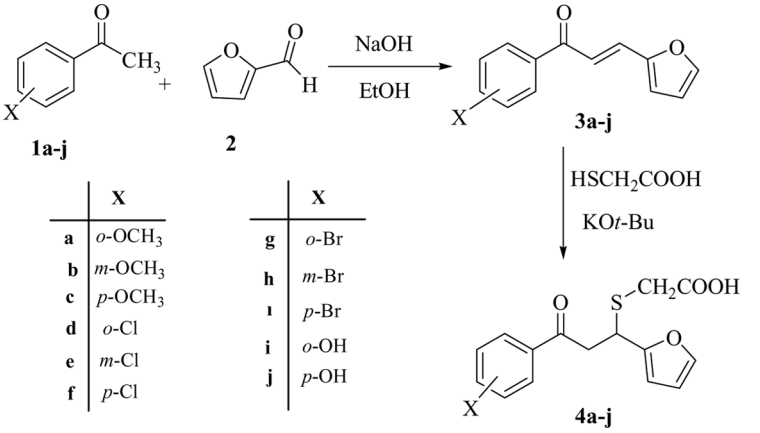


Scheme 1. Synthesis of chalcones (**3a–j**) and addition of thioglicolic acid.

After purification of the residue, chalcone derivatives (**3a–j**) were obtained in the yields of 69–97%. The compounds (**3a**,[19] **3b**,[20] **3c**,[20] **3f**,[20] **3ı**,[21] **3i**,[19] and **3j**[22]) are known in the literature as the others were synthesized for first time.

The structures of chalcone derivatives were evaluated using infrared (IR), ^{1}H NMR, and ^{13}C NMR spectroscopic methods.

A series of chalcone derivatives containing thioglicolic acid (**4a–j**) was prepared by the addition of thioglicolic acid to chalcones (**3a–j**). The reaction of chalcones **3a–j** with thioglicolic acid in the presence of KO*t*-Bu (6% mmol) at room temperature for 3 h gave solely the products (**4a–j**) of 1,4-addtion of thioglicolic acid in good yields. When this reaction is carried out in some solvent such as $CHCl_3$ or CH_2Cl_2, the yield decreases drastically even at very long reaction times (36 h).

The crude products were purified by filtration on a short silica-gel column and recrystallized from $CHCl_3$ or CH_2Cl_2/*n*-hexane (3:7). In this series, compounds (**4a–j**) were produced for the first time according to the literature.

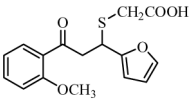
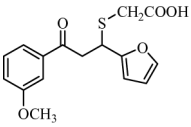
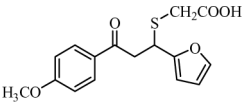
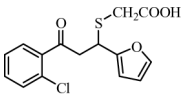
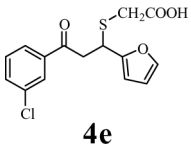
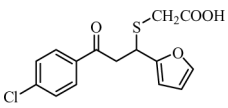
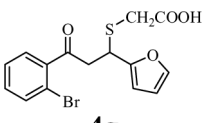
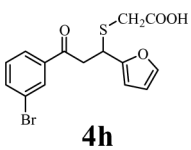
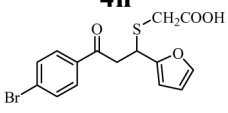
The structures of thioglicolic acid derivatives (**4a–j**) were also determined on the basis of spectral data (^{1}H NMR, ^{13}C NMR, IR, and elemental analysis). In the ^{1}H NMR spectra of **4a–j**, the protons of PhCO*CH*$_2$ led to an AB system that is characteristic to these compounds.[23] Part A of the AB system was shown as a doublet of doublet at $\delta = 3.76$–3.65 ($J = 17.2$–17.6, 7.8–8.4 Hz), and part B was a doublet of doublet at $\delta = 3.59$–3.53 ($J = 17.2$–17.6, 6.0–6.8 Hz). Moreover, in the ^{1}H NMR spectrum of **4a–j**, the protons of PhCOCH$_2$*CH* led to a doublet of doublet at $\delta = 4.83$–4.66 ($J = 7.7$–8.2, 6.0–6.9 Hz). All of the spectral data are consistent with the titled compounds.

In summary, a simple, convenient, and efficient method is reported for the addition of thioglicolic acid to chalcones. Additionally, potassium-tertiary-butoxide (KO*t*-Bu) is found as an efficient catalyst for Michael addition of thioglicolic acid to chalcone derivatives in solvent-free conditions.

EXPERIMENTAL

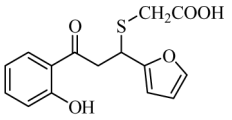
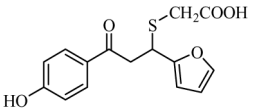
Melting points were measured on an Electrothermal 9100 apparatus. IR spectra (KBr disc or in $CHCl_3$) were recorded on a Jasco Fourier transform (FT)/IR-430

Table 1. Synthesized compounds **4a–j**

Entry	Product	Time (h)	Yield (%)	Mp (°C)
1	 **4a**	3	92	Viscous oil
2	 **4b**	3	88	Viscous oil
3	 **4c**	3	81	Viscous oil
4	 **4d**	3	94	Viscous oil
5	 **4e**	3	91	Viscous oil
6	 **4f**	3	85	91
7	 **4g**	3	77	Viscous oil
8	 **4h**	3	83	85
9	 **4ı**	3	93	Viscous oil

(*Continued*)

Table 1. Continued

Entry	Product	Time (h)	Yield (%)	Mp (°C)
10	 **4i**	3	86	137
11	 **4j**	3	79	145

spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 instrument. Tetramethylsilane (TMS) served as internal standard (δ 0.00) for ^{1}H NMR, and $CDCl_3$ (δ 77.0) was used for ^{13}C NMR spectroscopy; J values are given in hertz. The multiplicities of the signals in the ^{1}H NMR spectra are abbreviated as 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.

All column chromatographies were performed on silica gel (60–230 mesh, Merck).

General Procedure for the Synthesis of Chalcone 3a–j

Furfural (1 mmol) and NaOH (8 mL, 2.5 M NaOH) was added to a solution of acetophenone derivative (1 mmol) in ethanol (20 mL) at room temperature. The mixture was stirred for 3 h. Then, the mixture was extracted with $CHCl_3$ or CH_2Cl_2 and washed with dilute HCl. The organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by filtration on a short silica-gel column eluting with $CHCl_3$ or CH_2Cl_2/*n*-hexane (3:7) and/or crystallized in $CHCl_3$/*n*-hexane (3:7) or EtOH.

Data of 3d, 3e, 3g, and 3h

1-(2-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one (3d). Yield: 91%. Viscous oil. IR: (KBr cm^{-1}) 3126, 2925, 2852, 1621, 1598, 1301, 1284, 1016, 752. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.31 (m, 4H, ArH; 1 H, H2), 7.27–7.21 (d, J = 15.7 Hz, 1H, H7), 7.04–6.99 (d, J = 15.7 Hz, 1H, H6), 6.70–6.69 (d, J = 3.5 Hz, 1H, H4), 6.50–6.48 (dd, J = 3.4 1.8 Hz, 1H, H3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.30, 151.01, 145.59, 139.02, 132.03, 131.40, 131.26, 130.30, 129.30, 126.86, 123.58, 116.88, 112.85. Anal. calcd. for $C_{13}H_9O_2Cl$: C, 67.11; H, 3.90. Found: C, 67.40; H, 3.92.

1-(3-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one (3e). Yield: 78%. Mp 52–54 °C. IR: (KBr cm^{-1}) 3120, 3068, 2923, 2848, 1679, 1569, 1421, 1284, 1245,

1197, 1010, 730. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (t, J = 1.8 Hz, 1H), 7.87–7.91 (dt, J = 1.3 Hz, 1H), 7.51–7.52 (dd, J = 2.1, 1.1 Hz, 1H), 7.54–7.55 (d, J = 3.5 Hz, 1H), 7.58–7.63 (d, J = 15.3 Hz, 1H), 7.35–7.40 (d, J = 15.3 Hz, 1H), 6.75–6.72 (d, J = 3.4 Hz, 1H), 6.53–6.51 (dd, J = 3.4, 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.34, 151.46, 145.25, 139.71, 134.90, 132.66, 131.30, 129.94, 128.49, 126.48, 118.57, 116.90, 112.84. Anal. calcd. for $C_{13}H_9O_2C$: C, 67.11; H, 3.90. Found: C, 67.81; H, 3.97.

1-(2-Bromophenyl)-3-(furan-2-yl)prop-2-en-1-one (3g). Yield, 70%. Viscous oil. IR: (KBr cm^{-1}) 3116, 3048, 3008, 1646, 1624, 1600, 1301, 1282, 1014, 970, 754. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.06 (m, 4H, ArH), 7.35 (d, J = 1.5 Hz, 1H, H2), 7.05–7.01 (d, J = 15.8 Hz, 1H, H7), 6.82–6.78 (d, J = 15.8 Hz, 1H, H6), 6.52–6.51 (d, J = 3.5 Hz, 1H, H4), 6.31 (dd, J = 3.4, 1.8 Hz, Hz 1H, H3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.03, 150.89, 145.71, 140.98, 133.42, 132.36, 131.41, 129.10, 127.42, 123.37, 119.43, 117.03, 112.95. Anal. calcd. for $C_{13}H_9O_2Br$: C, 56.34; H, 3.27. Found: C, 56.62; H, 3.56.

1-(3-Bromophenyl)-3-(furan-2-yl)prop-2-en-1-one (3h). Yield: 79%. Mp 60–63 °C. IR: (KBr cm^{-1}) 3122, 2981, 2896, 1698, 1683, 1558, 1540, 1508, 1488, 773, 418. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (t, J = 1.7 Hz, 1H, H14), 7.91–7.87 (dt, J = 1.5 Hz, 1H, H10), 7.68–7.67 (dd as brd, J = 1.9, 1.1 Hz, 1H, H12), 7.61–7.56 (d, J = 15.3 Hz, 1H, H7), 7.53 (brd, J = 0.6 Hz, 1H, H2), 7.38–7.33 (t, J = 7.7 Hz, 1H, H11), 7.37–7.32 (d, J = 15.7 Hz, 1H, H6), 6.73–6.72 (d, J = 3.1 Hz, 1H, H4), 6.51–6.50 (dd, J = 1.8 Hz, 3.4 Hz 1H, H3).^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.18, 151.44, 145.27, 139.89, 135.56, 131.41, 131.30, 130.19, 126.92, 122.97, 118.51, 116.93, 112.86. Anal. calcd. for $C_{13}H_9O_2Br$: C, 56.34; H, 3.27. Found: C, 56.35; H, 3.46.

General Procedure for the Synthesis of 4a–j

A small amount of KO*t*-Bu (6 mmol) was added to a magnetically stirred mixture of chalcone derivatives (1 mmol) and thioglicolic acid (2 mmol and/or 3 mmol), and the reaction mixture was stirred at room temperature for 3 h. Then, the mixture was extracted with $CHCl_3$ and washed with dilute HCl. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by filtration on a short silica-gel column eluting with $CHCl_3$ or CH_2Cl_2/*n*-hexane (3:7) and/or crystallized in $CHCl_3$ or CH_2Cl_2/*n*-hexane (3:7).

Data of 4a–j

2-(1-(Furan–2-yl)-3-(2-methoxyphenyl)-3-oxopropylthio)acetic acid (4a). Yield: 92%. Viscous oil. IR: (CCl_4 cm^{-1}): 3716, 3414, 2553, 2219, 1759, 1714, 1689, 1641, 1416, 1256, 1195, 1108, 967, 764. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ = 9.59 (s, 1H, OH), 7.67 (dd, J = 7.8, 1.1 Hz, 1H, H10), 7.42 (t, J = 0.8 Hz, 1H, H12), 7.35 (m, 1H, H2), 7.00–6.95 (m, 2H, H11, H13), 6.28–6.24 (m, 2H, H3, H4), 4.79 (t, J = 7.2 Hz, 1H, H6), 3.92 (s, 3 H, OCH_3), 3.76 (dd, J = 17.6, 7.9 Hz, 1H, H7), 3.59 (dd, J = 17.6, 6.5 Hz,1H, H7), 3.21 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ = 198.7, 176.5, 151.2, 142.6, 137.1, 134.4, 130.9, 127.6, 124.5, 110.4, 108.8,

45.8, 45.7, 37.7, 32.6. Anal. calcd. for $C_{16}H_{16}O_5S$: C, 59.99; H, 5.03; S, 10.01. Found: C, 59.89; H, 4.98; S, 9.87.

2-(1-(Furan–2-yl)-3-(3-methoxyphenyl)-3-oxopropylthio)acetic acid (4b). Yield: 88%. Viscous oil. IR: (CCl_4 cm^{-1}): 3456, 3129, 2544, 2378, 1759, 1676, 1545, 1401, 1286, 1190, 1086, 994, 768. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 9.40$ (s, 1H, OH), 7.54–7.08 (m, 5H, H2, H10, H11, H12, H13), 6.28–6.27 (m, 2H, H3, H4), 4.83 (dd, $J = 8.2$, 6.0 Hz, 1H, H6), 3.83 (s, 3H, OCH_3), 3.75 (dd, $J = 17.4$, 8.2 Hz, 1H, H7), 3.54 ($J = 17.4$, 6.0 Hz, 1H, H7), 3.18 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 196.0$, 172.7, 159.8, 152.3, 142.3, 137.8, 129.6, 120.7, 119.9, 112.2, 110.3, 108.1, 55.4, 41.9, 37.5, 33.0. Anal. calcd. for $C_{16}H_{16}O_5S$: C, 59.99; H, 5.03; S, 10.01. Found: C, 59.86; H, 4.98; S, 9.93.

2-(1-(Furan–2-yl)-3-(4-methoxyphenyl)-3-oxopropylthio)acetic acid (4c). Yield: 81%. Viscous oil. IR: (CCl_4 cm^{-1}): 3826, 3424, 2946, 2758, 1768, 1740, 1678, 1545, 1416, 1265, 1206, 1119, 963, 747. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 8.52$ (s, 1H, OH), 7.94 (d, $J = 8.9$ Hz, 2H, AA′, H10, H13), 7.35 (t, $J = 1.3$ Hz, 1H, H2), 6.93 (d, $J = 8.9$ Hz, 2H, XX′, H11, H12), 6.29 (d, $J = 1.3$ Hz, 2H, H3, H4), 4.83 (dd, $J = 8.1$, 6.2 Hz, 1H, H6), 3.86 (s, 1H, OCH_3), 3.71 (dd, $J = 17.2$, 8.1 Hz, 1H, H7), 3.50 (dd, $J = 17.2$, 6.2 Hz, 1H, H7), 3.20 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 194.7$, 173.4, 163.7, 152.4, 142.3, 130.4, 129.5, 113.8, 110.2, 108.1, 55.5, 41.4, 37.8, 33.0. Anal. calcd. for $C_{16}H_{16}O_5S$: C, 59.99; H, 5.03; S, 10.01. Found: C, 59.66; H, 5.02; S, 9.87.

2-(3-(2-Cholorophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4d). Yield: 94%. Viscous oil. IR: (CCl_4 cm^{-1}): 3326, 2435, 1719, 1700, 1698, 1673, 1586, 1482, 1286, 1211, 1008, 961, 793. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 9.57$ (s, 1H, OH), 7.57–7.28 (m, 5H, H2, H10, H11, H12, H13), 6.30–6.28 (m, 2H, H3, H4), 4.76 (dd, $J = 14.6$, 7.6 Hz,1 H, H6), 3.73 (dd, $J = 17.3$, 7.8 Hz, 1H, H7), 3.56 ($J = 17.3$, 6.8 Hz, 1H, H7), 3.22 (s, 2H, H15).^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 199.2$, 176.1, 151.7, 142.6, 138.5, 132.2, 131.0, 130.5, 129.3, 127.0, 110.3, 108.5, 45.9, 38.0, 32.7. Anal. calcd. for $C_{15}H_{13}ClO_4S$: C, 55.47; H, 4.03; S, 9.87. Found: C, 55.40; H, 3.92; S, 9.77.

2-(3-(3-Cholorophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4e). Yield: 91%. Viscous oil. IR: (CCl_4 cm^{-1}): 3432, 2835, 1879, 1724, 1679, 1663, 1516, 1413, 1263, 1200, 1012, 991, 755. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 10.28$ (s, 1H, OH), 8.07 (d, $J = 1.7$ Hz, 1H, H14,), 7.87 (dt, $J = 7.8$, 1.3 Hz, 1H, H10), 7.69 (dq, 7.8, 1.0 Hz, 1H, H12), 7.37–7.35 (m, 2H, H11, H2), 6.31 (d, $J = 1.2$ Hz, 2H, H3, H4), 4.83 (dd, $J = 7.8$, 6.4 Hz, 1H, H6), 3.72 (dd, $J = 17.5$, 7.8 Hz, 1H, H7), 3.53 (dd, $J = 17.5$, 6.3 Hz, 1H, H7), 3.23 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 194.8$, 176.1, 151.7, 142.6, 138.0, 136.3, 131.2, 130.3, 126.6, 123.1, 110.3, 108.5, 41.8, 37.6, 32.8. Anal. calcd. for $C_{15}H_{13}ClO_4S$: C, 55.47; H, 4.03; S, 9.87. Found: C, 55.34; H, 3.84; S, 8.99.

2-(3-(4-Cholorophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4f). Yield: 85%. Mp 91 °C. IR: (CCl_4 cm^{-1}): 3621, 3244, 2654, 2315, 1763, 1726, 1698, 1564, 1421, 1276, 1200, 1108, 982, 784. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 9.5$ (s, 1H, OH), 10.5 (s, 1H, OH), 7.91 (d, $J = 6.7$ Hz, 2H, AA′, H10, H14), 7.45 (d,

$J = 6.7$ Hz, 2H, XX′, H11, H12), 7.38–7.37 (m, 1H, H2), 6.31–6.30 (m, 2H, H3, H4), 4.84 (dd, $J = 7.8$, 6.4 Hz, 1H, H6), 3.74 (dd, $J = 17.4$, 7.8 Hz, 1H, H7), 3.55 (dd, $J = 17.4$, 6.4 Hz, 1H, H7), 3.24 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 194.9$, 175.9, 151.7, 142.6, 140.0, 134.6, 129.5, 129.0, 110.3, 108.5, 41.7, 37.7, 32.8. Anal. calcd. for $C_{15}H_{13}ClO_4S$: C, 55.47; H, 4.03; S, 9.87. Found: C, 55.40; H, 4.00; S, 9.72.

2-(3-(2-Bromophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4g). Yield: 77%. Viscous oil. IR: (CCl_4 cm^{-1}): 3232, 2697, 2318, 1766, 1736, 1685, 1541, 1329, 1376, 1210, 1185, 993, 752. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 9.7$ (s, 1H, OH), 7.80 (dd, $J = 7.6$, 0.9 Hz, 1H, H10), 7.37–7.31 (m, 4H, H2, H11, H12, H13), 6.31–6.29 (m, 2H, H3, H4), 4.78 (dd, $J = 7.8$, 6.9 Hz, 1H, H6), 3.70 ($J = 17.3$, 7.9 Hz, 1H, H7), 3.54 ($J = 17.3$, 6.8 Hz, 1H, H7), 3.22 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 199.9$, 176.2, 151.5, 142.6, 140.7, 133.7, 132.0, 128.8, 127.5, 118.7, 110.3, 108.6, 45.7, 37.9, 32.7. Anal. calcd. for $C_{15}H_{13}BrO_4S$: C, 48.79; H, 3.55; S, 8.68. Found: C, 48.40; H, 3.38; S, 8.61.

2-(3-(3-Bromophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4h). Yield: 83%. Mp 85 °C. IR: (CCl_4 cm^{-1}): 3342, 2974, 2188, 1754, 1719, 1698, 1532, 1387, 1205, 1152, 945, 786. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 11.02$ (s, 1H, OH), 7.91 (d, $J = 1.7$ Hz, 1H, H14), 7.83 (d, $J = 7.8$ Hz, 1H, H10), 7.56–7.53 (m, 1H, H12), 7.44–7.37 (m, 2H, H11, H2), 6.31 (d, $J = 0.6$ Hz, 2H, H3, H4), 4.84 (dd, $J = 7.7$, 6.5 Hz, 1H, H6), 3.74 (dd, $J = 17.5$, 7.8 Hz, 1H, H7), 3.54 (dd, $J = 17.5$, 6.3 Hz, 1H, H7), 3.24 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 194.9$, 176.4, 151.7, 142.6, 137.8, 135.0, 133.4, 130.0, 128.2, 126.2, 110.3, 108.5, 41.8, 37.6, 32.8. Anal. calcd. for $C_{15}H_{13}BrO_4S$: C, 48.79; H, 3.55; S, 8.68. Found: C, 48.65; H, 3.52; S, 8.77.

2-(3-(4-Bromophenyl)-1-(furan–2-yl)-3-oxopropylthio)acetic acid (4i). Yield: 93%. Viscous oil. IR: (CCl_4 cm^{-1}): 3352, 2743, 2186, 1798, 1765, 1653, 1541, 1325, 1369, 1220, 1153, 981, 788. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 10.7$ (s, 2H, OH), 7.82 (d, $J = 8.5$ Hz, 2H, AA′, H10, H13), 7.62 (d, $J = 8.5$ Hz, 2H, XX′, H11, H12), 7.37 (t, $J = 1.3$ Hz, 1H, H2), 6.31 (d, $J = 1.3$ Hz, 2H, H3, H4), 4.84 (dd, $J = 7.7$, 6.5 Hz, 1H, H6), 3.73 (dd, $J = 17.4$, 7.8 Hz, 1H, H7), 3.53 (dd, $J = 17.4$, 6.4 Hz, 1H, H7), 3.23 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 195.2$, 176.3, 151.7, 142.6, 135.0, 132.0, 129.6, 128.8, 110.3, 108.5, 41.6, 37.7, 32.8. Anal. calcd. for $C_{15}H_{13}BrO_4S$: C, 48.79; H, 3.55; S, 8.68. Found: C, 48.74; H, 3.47; S, 8.59.

2-(1-(Furan–2-yl)-3-(2-hydroxyphenyl)-3-oxopropylthio)acetic acid (4i). Yield: 86%. Mp 137 °C. IR: (CCl_4 cm^{-1}): 3423, 2375, 2339, 1714, 1702, 1695, 1637, 1508, 1490, 1486, 1282, 1218, 1010, 981, 771. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta = 12.0$ (s, 1H, OH), 7.80 (dd, $J = 8.0$, 1.4 Hz, 1H, H10,), 7.41–7.36 (m, 1H, H12), 7.28 (dd, $J = 1.8$, 0.9 Hz, 1H, H2), 6.85–6.80 (m, 2H, H11, H13), 6.22–6.19 (m, 2H, H3, H4), 4.74 (dd, $J = 8.1$, 6.1 Hz, 1H, H6), 4.54 (s, 1H, OH), 3.73 (dd, $J = 17.4$, 8.1 Hz, 1H, H7), 3.58 (dd, $J = 17.4$, 6.2 Hz, 1H, H7), 3.10 (s, 2H, H15). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta = 207.7$, 176.5, 167.5, 157.6, 141.8, 135.4, 124.4, 123.3, 115.5, 113.0, 46.7, 42.4, 37.7, 35.2. Anal. calcd. for $C_{15}H_{14}O_5S$: C, 58.81; H, 4.61; S, 10.47. Found: C, 58.78; H, 4.55; S, 10.23.

2-(1-(Furan–2-yl)-3-(4-hydroxyphenyl)-3-oxopropylthio)acetic acid (4j). Yield: 79%. Mp 145 °C IR: (CCl_4 cm^{-1}): 3416, 2254, 2239, 1718, 1716, 1698, 1643, 1521, 1486, 1276, 1211, 1003, 989, 768. ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 12.4$ (s, 1H, OH), 10.5 (s, 1H, OH), 7.84 (d, $J = 8.7$ Hz, 2H, AA′, H10, H13), 7.50 (d, $J = 0.9$ Hz, 1H, H2), 6.82 (d, $J = 8.6$ Hz, 2H, XX′, H11, H12), 6.31 (d, $J = 1.8$ Hz, 1H, H3), 6.26 (d, $J = 3.0$ Hz, 1H, H4), 4.66 (dd, $J = 8.2$, 6.0 Hz, 1H, H6), 3.65 (dd, $J = 17.3$, 8.4 Hz, 1H, H7), 3.57 (dd, $J = 17.3$, 6.0 Hz, 1H, H7), 3.20 (s, 2H, H15). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): $\delta = 194.7$, 171.7, 162.7, 153.6, 142.6, 131.0, 128.2, 115.6, 110.7, 107.6, 40.5, 39.4, 33.0. Anal. calcd. for $C_{15}H_{14}O_5S$: C, 58.81; H, 4.61; S, 10.47. Found: C, 58.78; H, 4.58; S, 10.38.

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