The Catalytic Synthesis of Carboniolamide: the Role of sp³

Hybridized Oxygen

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**General:** $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker Avance II 400 spectrometer and resolved with MestreNova. IR spectra were recorded on ThermoFisher Nicolet iS5. Diethyl ether, acetone and EA were delivered from Innovation Technology solvent system. Column chromatography was performed on silica gel from Qingdao Marine Chemical Industry. Solvents used for chromatography were AR grade, as appropriate. All other solvents were distilled from commercial available source. All reactions were carried out in flame dried flask under common air atmosphere.

**Synthesis of glyoxylate:**

Benzyl glyoxylate:

A mixture of L-tartaric acid (20 g, 0.12 mol), benzyl alcohol (60 g, 0.6 mol), and $p$-TsOH (0.35 g, 2 mmol) in toluene (80 mL) was refluxed with a Dean-Stark, until no more water generated. After the removal of toluene and benzyl alcohol under reduced pressure, the residue was used in next step without further purification.

To a solution of dibenzyl L-tartrate (8.3 g, 25 mmol) in 60 mL of diethyl ether was added periodic acid dihydrate (5.7 g, 25 mmol), and the solution was stirred at room temperature for 15 minutes. After filtration, the filtrate was washed with saturated NaHCO$_3$ (15 mL) and brine (15 mL). Then the organic layer was dried (MgSO$_4$) and concentrated to offer the benzyl glyoxylate as a colorless oil, 8.2 g. The compound was used in the catalysis without further purification $^1$H NMR (400 MHz, D$_2$O) $\delta$ 7.58–7.30 (m, 5H), 5.30 (s, 1H), 5.19 (d, $J$ = 5.5 Hz, 2H).

Isopropyl glyoxylate:
To a solution of diisopropyl L-tartrate (40 mmol) in H₂O (20 mL) was added a solution of NaIO₄ (9.1 g, 40 mmol) in H₂O (50 mL) at 0 °C under nitrogen. After being stirred for 2 hours at 0 °C, the reaction mixture was warmed to room temperature and extracted with ethyl acetate. The combined organic layers were dried (MgSO₄) and concentrated under reduced pressure to offer colorless oil 9.3 g. It was pure enough and used in the catalysis directly without further purificatin. 

¹H NMR (400 MHz, D₂O) δ 5.20 (s, 1H), 4.93-4.99 (m, H), 1.19 (d, J = 6.3 Hz, 6H).

**General procedure for the catalysis**

To a reaction vial charged with amide (1.0 mmol), glyoxylate (1.0 mmol), and diphenyl hydrogen phosphate (25.0 mg, 0.1mmol) was added diethyl ether. Then the sealed reaction mixture was stirred at room temperature for specified time. The achieved slurry was then filtered, and the precipitate was washed with minimum amount of cold diethyl ether to give the compound as white powder.

**Analytical Data for product 1:**

![Diagram](image)

Ethyl 2-acetamido-2-hydroxyacetate 1a

Compound was prepared from aceticamide (59.1 mg, 1 mmol) and ethyl glyoxylate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 85%.

¹H NMR (400 MHz, D6-DMSO) δ 8.73 (d, J = 8.3 Hz, 1H), 6.47 (d, J = 6.3 Hz, 1H), 5.44 (dd, J = 8.4, 6.4 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 1.84 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H).

¹³C NMR (101 MHz, D6-DMSO) δ 169.94, 169.29, 71.05, 60.71, 22.54, 14.02.

IR(thin film cm⁻¹): 1087, 1107, 1238, 1293, 1350, 1374, 1393, 1547, 1649, 1657, 1737, 3315, 3413

ESI (M-H⁻), calc. for 184, found: 184.

HRMS, ESI(M÷Na⁺), calc. for (C₁₁H₁₃NO₄Na) : 184.0586, found: 184.0580.

m.p.101.1 -103.3 °C.
Ethyl 2-hydroxy-2-isobutyramidoacetate 1b

Compound was prepared from isobutyramide (87 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 83%.

\[\text{H NMR (400 MHz, D6-DMSO)} \delta 8.64 \text{ (d}, J = 8.3 \text{ Hz}, 1\text{H}), 5.43 \text{ (d}, J = 8.4 \text{ Hz}, 1\text{H}), 4.14-4.08 \text{ (m}, 2\text{H}), 2.46-2.40 \text{ (m}, 1\text{H}), 1.19 \text{ (t}, J = 7.1 \text{ Hz}, 3\text{H}), 0.99 \text{ (dd}, J = 6.8, 3.0 \text{ Hz}, 6\text{H}).\]

\[\text{C NMR (101 MHz, D6-DMSO)} \delta 176.50, 170.44, 71.55, 61.06, 34.01, 19.77, 19.58, 14.45.\]

IR (thin film cm\(^{-1}\)): 1078, 1107, 1374, 1547, 1649, 1657, 3315

ESI(M-H\(^{-}\)), calc. for 188, found:188.

HRMS, ESI(M+Na\(^{+}\)), calc. For (C\(_8\)H\(_{15}\)NO\(_3\)Na) 212.0899, found:212.0896.

m.p.90.9-92.7 \(^\circ\)C.

Ethyl 2-hydroxy-2-(2-phenylacetamido)acetate 1c

Compound was prepared from 2-phenylacetamide (135 mg, 1.0 mmol) and ethyl glyoxylate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 81%.

\[\text{H NMR (400 MHz, DMSO)} \delta 9.00 \text{ (d}, J = 8.4 \text{ Hz}, 1\text{H}), 7.40-7.11 \text{ (m}, 5\text{H}), 6.60 \text{ (d}, J = 6.4 \text{ Hz}, 1\text{H}), 5.45 \text{ (dd}, J = 8.3, 6.5 \text{ Hz}, 1\text{H}), 4.11 \text{ (q}, J = 7.1 \text{ Hz}, 2\text{H}), 1.18 \text{ (t}, J = 7.1 \text{ Hz}, 3\text{H}).\]

\[\text{C NMR (101 MHz, DMSO)} \delta 170.51, 170.27, 136.37, 129.51, 128.61, 126.85, 71.69, 61.18, 42.40, 14.41.\]

IR (thin film cm\(^{-1}\)): 1062, 1082, 1111, 1145, 1237, 1271, 1319, 1344, 1535, 1649, 1657, 1730, 1737, 3327, 3415.

ESI (M-H\(^{-}\)), calc. for 236, found: 236.

HRMS, ESI (M+Na\(^{+}\)), calc. for (C\(_{12}\)H\(_{15}\)NO\(_4\)Na) 260.0899, found: 260.0897.

m.p. 112.1-114.6 \(^\circ\)C.
Ethyl 2-benzamido-2-hydroxyacetate 1d

Compound was prepared from benzamide (242 mg, 2.0 mmol) and ethyl glyoxylate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 16 hours in the yield of 84%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 9.35 (d, $J = 7.8$ Hz, 1H), 7.99-7.80 (m, 2H), 7.68-7.37 (m, 3H), 6.57 (s, 1H), 5.65 (d, $J = 7.6$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H). The $^1$H NMR data matches with the reported value ² (where is the reference 2 as well as ref. 1?)

IR (thin film cm⁻¹): 692, 1039, 1094, 1152, 1226, 1294, 1313, 1346, 1447, 1471, 1535, 1648, 1754, 3312.

ESI (M-H⁻), calc. for 222, found: 222.

HRMS, ESI (M+Na⁺), calc. for (C₁₁H₁₃NO₄Na): 246.0743, found: 246.0740.

m.p. 108.5-110.3 °C

Ethyl 2-hydroxy-2-(4-methoxybenzamido)acetate 1e

Compound was prepared from 4-methoxybenzamide (151 mg, 1.0 mmol) and ethyl glyoxylate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 84%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 9.20 (d, $J = 7.8$ Hz, 1H), 7.90 (d, $J = 8.7$ Hz, 2H), 7.01 (d, $J = 8.7$ Hz, 2H), 6.52 (d, $J = 6.1$ Hz, 1H), 5.63 (t, $J = 6.8$ Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 1.20 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 170.53, 165.85, 162.37, 129.91, 126.11, 114.00, 72.31, 61.16, 55.83, 14.50.

IR (thin film cm⁻¹): 1025, 1038, 1090, 1176, 1229, 1265, 1322, 1344, 1510, 1536, 1546, 1611, 1641, 1753

ESI (M-H⁻), calc. for 252, found: 252.

HRMS, ESI (M+Na⁺), calc. for (C₁₂H₁₅NO₃Na): 276.0848, found: 276.0849.
m.p. 123.7-125.1 °C

![Diagram of molecule](image)

**1f**

**Ethyl 2-(4-fluorobenzenamido)-2-hydroxyacetate 1f**

Compound was prepared from 4-fluorobenzenamide (139 mg, 1.0 mmol) and ethyl glyoxylate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 91%.

$^1$H NMR (400 MHz, D6-DMSO) δ 9.38 (d, $J = 7.8$ Hz, 1H), 7.98 (dd, $J = 8.6$, 5.6 Hz, 2H), 7.32 (t, $J = 8.8$ Hz, 2H), 6.60 (d, $J = 6.5$ Hz, 1H), 5.64 (t, $J = 7.1$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 170.32, 165.36, 161.87, 130.76, 130.67, 127.55, 115.87, 115.66, 72.44, 61.23, 14.50.

IR (thin film cm$^{-1}$): 1039, 1095, 1150, 1158, 1219, 1245, 1290, 1317, 1348, 1503, 1544, 1603, 1642, 1746, 3321.

ESI (M-H$^-$), calc. for 240, found: 240.

HRMS, ESI (M+Na$^+$), calc. for (C$_{11}$H$_{13}$FNO$_4$Na): 264.0648. found: 264.0644.

![Diagram of molecule](image)

**1g**

**Ethyl 2-(4-chlorobenzenamido)-2-hydroxyacetate 1g**

Compound was prepared from 4-chlorobenzenamide (156mg, 1 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1 mmol) in diethyl ether 4 mL with the general procedure during 22 hours in the yield of 80%.

$^1$H NMR (400 MHz, D6-DMSO) δ 9.46 (d, $J = 7.8$ Hz, 1H), 7.92 (d, $J = 8.5$ Hz, 2H), 7.56 (d, $J = 8.5$ Hz, 2H), 6.63 (d, $J = 6.1$ Hz, 1H), 5.64 (t, $J = 6.9$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H).
$^{13}$C NMR (101 MHz, D6-DMSO) δ 170.26, 165.43, 137.01, 132.72, 129.93, 128.92, 72.44, 61.25, 14.49.
IR (thin film cm$^{-1}$): 1015, 1033, 1102, 1155, 1239, 1312, 1345, 1487, 1536, 1598, 1649, 1655, 1746, 3304, 3402.
LC-MS, ESI (M+Na$^+$), calc. for 280, found: 280.
HRMS, ESI (M+Na$^+$), calc. for (C$_{11}$H$_{12}$ClNO$_3$Na) 280.0353, found: 280.0356.
m.p. 106.2-108.1 °C.

![Image 1h]

1h

Ethyl 2-hydroxy-2-(4-(trifluoromethyl)benzamido)acetate 1h

Compound was prepared from 4-(trifluoromethyl)benzamide (189 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 μL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 80%.

$^1$H NMR (400 MHz, D6-DMSO) δ 9.62 (d, J = 7.8 Hz, 1H), 8.09 (d, J = 8.1 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 5.67 (d, J = 7.8 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 1.21 (t, J = 7.1 Hz, 3H).
$^{13}$C NMR (101 MHz, D6-DMSO) δ 170.15, 165.38, 137.76, 128.90, 125.87, 125.84, 72.50, 61.30, 14.47.
IR (thin film cm$^{-1}$): 1070, 1108, 1135, 1167, 1233, 1408, 1535, 1545, 1649, 1753, 3322.
ESI (M+Na$^+$), calc. for 314, found: 314.
HRMS, ESI (M+Na$^+$), calc. for (C$_{12}$H$_{13}$F$_3$NO$_3$Na) 314.0616, found: 314.0619.
m.p. 112.3-114.1 °C.

![Image 1i]

1i

Ethyl 2-(4-ethynylbenzamido)-2-hydroxyacetate 1i

Compound was prepared from 4-ethynylbenzamide (145 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 μL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 73%.
$^1$H NMR (400 MHz, D6-DMSO) δ 9.45 (d, $J = 7.8$ Hz, 1H), 7.77 (dd, $J = 56.2$, 8.5 Hz, 4H), 6.62 (d, $J = 6.5$ Hz, 1H), 5.73 – 5.56 (m, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 170.24, 165.56, 133.09, 131.87, 130.11, 125.97, 72.43, 61.25, 14.49.

IR (thin film cm$^{-1}$): 1033, 1097, 1150, 1228, 1316, 1350, 1536, 1591, 1642, 1649, 1656, 1753, 3327.

ESI (M+Na$^+$), calc. for 270, found: 270.

HRMS, ESI (M+Na$^+$), calc. for (C$_{15}$H$_{15}$NO$_4$Na) 270.0743, found: 270.0740.

m.p. 118.3-120.1 °C.

![Structure 1j](image)

**1j**

**Ethyl 2-cinnamamido-2-hydroxyacetate 1j**

Compound was prepared from cinnamamide (147 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 81%.

$^1$H NMR (400 MHz, D6-DMSO) δ 8.95 (d, $J = 8.4$ Hz, 1H), 7.86 – 7.26 (m, 6H), 6.74 (d, $J = 15.8$ Hz, 1H), 6.66 (d, $J = 5.7$ Hz, 1H), 5.60 (dd, $J = 7.6$, 5.5 Hz, 1H), 4.14 (q, $J = 7.1$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 169.84, 164.66, 140.08, 134.68, 129.76, 129.00, 127.68, 121.47, 71.32, 60.85, 14.04.

IR (thin film cm$^{-1}$): 724, 764, 969, 975, 1021, 1072, 1093, 1113, 1195, 1208, 1328, 1347, 1369, 1425, 1449, 1469, 1536, 1547, 1630, 1650, 1657, 1753, 3289.

ESI (M+Na$^+$), calc. for 272, found:272.

HRMS, ESI (M+Na$^+$), calc. for(C$_{15}$H$_{15}$NO$_4$Na) 272.0899, found:272.0900.

m.p.115.4-118.1 °C.

![Structure 1k](image)

**1k**

**Ethyl 2-acrylamido-2-hydroxyacetate 1k**

Compound was prepared from acrylamide (71 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1 mmol) in diethyl ether 4 mL with the general procedure during 22 hours in the yield of 81%.
$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 8.98 (d, $J = 8.2$ Hz, 1H), 6.64 (d, $J = 6.2$ Hz, 1H), 6.30-6.12 (m,2H), 5.65 (d, $J = 10.1$ Hz, 1H), 5.53 (t, $J = 7.2$ Hz, 1H), 4.11 (q, $J = 7.0$ Hz, 2H), 1.19 (t, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 169.77, 164.24, 131.15, 126.73, 71.25, 60.82, 14.02.

IR (thin film cm$^{-1}$): 1063, 1100, 1221,1252, 1306, 1352, 1370, 1414, 1535, 1546, 1630, 1665, 1744, 3313, 3401.

ESI (M-H$^-$), calc. for 172, found: 172.

HRMS, ESI (M+Na$^+$), calc. for (C$_3$H$_7$NO$_3$Na) 196.0586, found:196.0583.

m.p. 79.1-80.6 °C.

![Structure 1i](image)

**1i**

Ethyl 2-hydroxy-2-(thiophen-3-yl)acetamido)acetate **1i**

Compound was prepared from 2-thiopheneacetamide (141 mg, 1mmol) and ethyl glyoxalate (50% in toluene, 198 μL, 1 mmol) in diethyl ether 4 mL with the general procedure during 20 hours in the yield of 83%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 9.02 (d, $J = 8.3$ Hz, 1H), 7.37 (dd, $J = 5.1$, 1.2 Hz, 1H), 7.02 – 6.87 (m, 2H), 6.65 (d, $J = 6.5$ Hz, 1H), 5.45 (dd, $J = 8.3$, 6.5 Hz, 1H), 4.12 (q, $J = 7.1$ Hz, 2H), 3.71 (s, 2H), 1.19 (t, $J = 7.1$ Hz, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 170.16, 169.49, 137.41, 126.99, 126.67, 125.40, 71.75, 61.24, 36.59, 14.43.

IR (thin film cm$^{-1}$): 700, 986, 1066, 1099, 1191, 1215, 1246, 1342, 1403, 1535, 1666, 1743, 2979, 3313, 3404.

ESI (M-H$^-$), calc. for 242, found:242.

HRMS, ESI (M+Na$^+$), calc. for(C$_{10}$H$_{13}$NO$_3$SNa) 266.0463, found:266.0462

m.p. 96.5-98.1 °C.

![Structure 1m](image)

**1m**
Ethyl 2-(((benzylcarbonyl)amino)-2-hydroxyacetate 1m

Compound was prepared from Cbz-NH₂ (159 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 80%.

¹H NMR (400 MHz, D6-DMSO) δ 8.27 (d, J = 8.3 Hz, 1H), 7.42 – 7.29 (m, 5H), 6.47 (d, J = 6.5 Hz, 1H), 5.38 – 5.17 (m, 1H), 5.17 – 4.93 (m, 2H), 4.11 (q, J = 7.0 Hz, 2H), 1.20 (t, J = 7.1 Hz, 3H).

¹³C NMR (101 MHz, D6-DMSO) δ 170.00, 155.89, 137.26, 128.82, 128.35, 128.29, 73.75, 66.03, 61.24, 14.44.

IR (thin film cm⁻¹): 754, 984, 1011, 1027, 1084, 1110, 1215, 1258, 1354, 1442, 1536, 1697, 1754, 2978, 3336.

ESI (M+Na⁺), Calc. for 276. Found: 276.

HRMS, ESI (M+Na⁺), calc. for (C₁₂H₁₅NO₃Na) 276.0848, found: 276.0844.

m.p. 77.6-79.3°C.

![Structural formula of 1m](image1)

Ethyl 2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-2-hydroxyacetate 1n

Compound was prepared from Fmoc-NH₂ (239 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µL, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 90%.

¹H NMR (400 MHz, D6-DMSO) δ 8.43 (d, J = 8.6 Hz, 1H), 7.90 (d, J = 7.5 Hz, 2H), 7.74 (t, J = 8.1 Hz, 2H), 7.32-7.45 (m, 4H), 6.50 (s, 1H), 5.29 (d, J = 8.6 Hz, 1H), 4.36 – 4.20 (m, 3H), 4.13 (q, J = 7.1 Hz, 2H), 1.21 (t, J = 7.1 Hz, 3H).

¹³C NMR (101 MHz, D6-DMSO) δ 170.04, 155.92, 144.24, 144.14, 141.18, 128.14, 127.54, 125.83, 125.76, 120.59, 73.73, 66.34, 61.25, 46.94, 14.47.

IR (thin film cm⁻¹): 740, 758, 1042, 1093, 1224, 1267, 1331, 1449, 1530, 1703, 1721, 1753, 3328.

ESI (M+H⁺), calc. for 340, found: 340.

HRMS, ESI (M+Na⁺), calc. for(C₁₉H₁₉NO₃Na) 364.1161, found:364.1163.

m.p. 125.3-127.1 °C.
Isopropyl 2-benzamido-2-hydroxyacetate 1o

Compound was prepared from benzamide (121 mg, 1 mmol) and isopropyl glyoxalate (116 mg, 1 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 80%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 9.32 (d, $J = 7.8$ Hz, 1H), 8.01 – 7.79 (m, 2H), 7.46–7.58 (m, 3H), 6.53 (d, $J = 6.6$ Hz, 1H), 5.59 (dd, $J = 7.6, 6.7$ Hz, 1H), 4.92–4.99 (m, 1H), 1.36 – 1.04 (m, 6H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 169.88, 166.43, 134.03, 132.11, 128.80, 127.96, 72.48, 68.74, 21.97.

IR (thin film cm$^{-1}$): 693, 729, 1037, 1098, 1153, 1226, 1294, 1313, 1353, 1374, 1451, 1536, 1642, 1747, 3328.

ESI (M-H$^-$), calc. for 236, found: 236.

HRMS, ESI (M+Na$^+$), calc. for (C$_{12}$H$_8$NO$_4$Na) : 260.0899, found: 260.0896.

m.p. 120.9–122.6$^\circ$C.

Isopropyl 2-(((benzoyloxy)carbonyl)amino)-2-hydroxyacetate 1p

Compound was prepared from Cbz-NH$_2$ (239 mg, 1.0 mmol) and isopropyl glyoxalate (116 mg, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 80%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 8.27 (d, $J = 8.5$ Hz, 1H), 7.44 – 7.29 (m, 5H), 6.44 (d, $J = 6.5$ Hz, 1H), 5.22 (dd, $J = 8.3, 6.8$ Hz, 1H), 5.12 – 4.98 (m, 2H), 4.88–4.94 (m 1H), 1.19 (t, $J = 6.9$ Hz, 6H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 169.49, 155.87, 137.29, 128.81, 128.33, 128.26, 73.84, 68.81, 65.98, 21.91, 21.89.

IR (thin film cm$^{-1}$): 750, 991, 1013, 1089, 1227, 1262, 1341, 1376, 1406, 1528, 1697, 1743, 3349, 3404.

ESI (M-H$^-$), calc. for 268, found: 268.

HRMS, ESI (M+Na$^+$), calc. for(C$_{13}$H$_{17}$NO$_3$Na) 290.1005, found:290.1003.
m.p. 108.4-110.1 °C.

![Structure 1q]

Isopropyl 2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-2-hydroxyacetate 1q

Compound was prepared from fmoc-NH2 (239 mg, 1 mmol) and isopropyl glyoxalate (116 mg, 1 mmol) in diethyl ether 4 mL with the general procedure during 22 hours in the yield of 85%.

$^1$H NMR (400 MHz, D6-DMSO) δ 8.41 (d, $J = 8.6$ Hz, 1H), 7.90 (d, $J = 7.5$ Hz, 2H), 7.84 – 7.65 (m, 2H), 7.45-7.31 (m, 4H), 6.46 (d, $J = 6.4$ Hz, 1H), 5.35 – 5.13 (m, 1H), 4.95-4.90 (m, 1H), 4.40 – 4.07 (m, 3H), 1.21 (t, $J = 5.5$ Hz, 6H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 169.54, 155.92, 144.23, 144.14, 141.18, 141.15, 128.14, 127.53, 125.84, 125.76, 120.59, 73.82, 68.82, 66.34, 46.93, 21.93.

IR(thin film cm⁻¹): 740, 759, 990, 1094, 1226, 1266, 1335, 1375, 1450, 1529, 1702, 1726, 1745, 3335, 3398.

ESI (M+Na⁺), calc. for 378, found:378.

HRMS, ESI (M+Na⁺), calc. for (C$_{26}$H$_{31}$NO$_3$Na) 378.1318, found 378.1317.

m.p. 169.1-171.5 °C.

![Structure 1r]

Eenzyll 2-hydroxy-2-(4-methylbenzamido)acetate 1r

Compound was prepared from p-toluamide(135 mg, 1 mmol) and benzyl glyoxalate (168 mg, 1 mmol) in diethyl ether 4 mL with the general procedure during 24 hours in the yield of 78%.

$^1$H NMR (400 MHz, D6-DMSO) δ 9.36 (d, $J = 7.8$ Hz, 1H), 7.81 (d, $J = 8.1$ Hz, 2H), 7.44 – 7.27 (m, 7H), 5.70 (d, $J = 7.8$ Hz, 1H), 5.17 (s, 2H), 2.36 (d, $J = 4.7$ Hz, 3H).
$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 170.37, 166.36, 142.13, 136.35, 131.14, 129.34, 128.83, 128.48, 128.30, 128.02, 72.46, 66.55, 21.45.
IR (thin film cm$^{-1}$): 696, 1093, 1153, 1217, 1316, 1345, 1502, 1536, 1543, 1612, 1641, 1656, 1753, 3308.
ESI (M+Na$^+$), calc. for 322, found: 322.
HRMS, ESI (M+Na$^+$), calc. for (C$_{12}$H$_{13}$NO$_4$Na) 322.1056, found: 322.1057.
m.p. 109.2-110.7 °C.

![Diagram 1](image1.png)

1s

Eenzy1 2-hydroxy-2-(thiophene-3-carboxamido)acetate 1s

Compound was prepared from 2-thiophenecarboxamide (127 mg, 1.0 mmol) and benzyl glyoxalate (168 mg, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 80%.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 9.46 (d, $J = 7.9$ Hz, 1H), 7.87 (dd, $J = 40.7, 4.0$ Hz, 2H), 7.49 – 7.26 (m, 5H), 7.17 (dd, $J = 4.8, 4.0$ Hz, 1H), 6.75 (d, $J = 6.4$ Hz, 1H), 5.70 (dd, $J = 7.7, 6.6$ Hz, 1H), 5.31 – 5.09 (m, 2H).
$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 170.15, 161.33, 139.45, 136.28, 132.21, 129.62, 128.85, 128.55, 128.51, 128.32, 72.35, 66.62.
IR(thin film cm-1): 730, 1065, 1086, 1134, 1196, 1210, 1280, 1327, 1359, 1421, 1513, 1535, 1545, 1639, 1764.
ESI(M+Na$^+$), calc. for 314, found: 314.
HRMS, ESI (M+Na$^+$), calc. for (C$_{14}$H$_{13}$NO$_4$SNa) 314.0463, found: 314.0461.
m.p. 99.5-101.2 °C.

![Diagram 2](image2.png)

1t
Benzyl 2-(((9H-fluoren-9-ylmethoxy)carbonyl)amino)-2-hydroxyacetate 1t

Compound was prepared from fmod-NH2 (239 mg, 1.0 mmol) and benzyl glyoxalate (168 mg, 1.0 mmol) in diethyl ether 4 mL with the general procedure during 18 hours in the yield of 88%.

$^1$H NMR (400 MHz, D6-DMSO) δ 8.51 (d, $J = 8.6$ Hz, 1H), 7.90 (d, $J = 7.5$ Hz, 2H), 7.82 – 7.64 (m, 2H), 7.55 – 7.20 (m, 9H), 6.61 (s, 1H), 5.37 (d, $J = 8.6$ Hz, 1H), 5.17 (s, 2H), 4.43 – 4.10 (m, 3H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 169.96, 155.94, 144.22, 144.13, 141.16, 136.23, 128.85, 128.54, 128.40, 128.14, 127.54, 125.82, 125.74, 120.59, 73.84, 66.63, 66.40, 46.93.

IR (thin film cm$^{-1}$): 697, 739, 759, 988, 1016, 1090, 1217, 1266, 1350, 1450, 1530, 1702, 1721, 1747, 3331.

ESI (M+H$^+$), calc. for 482, found: 482.

HRMS, ESI (M+Na$^+$), calc. for (C$_{36}$H$_{27}$NO$_3$Na) 504.1787, found: 504.1785.

m.p. 128.1-130.0 °C.

![Structure of 1t](image)

Benzyl 2-(((benzyloxy)carbonyl)amino)-2-hydroxyacetate 1u

Compound was prepared from cbz-NH2 (159 mg, 1 mmol) and benzyl glyoxalate (168 mg, 1 mmol) in diethyl ether 4 mL with the general procedure during 22 hours in the yield of 60%. $^1$H NMR (400 MHz, D6-DMSO) δ 8.35 (d, $J = 8.4$ Hz, 1H), 7.32-7.38 (m,10H), 6.57 (d, $J = 6.4$ Hz, 1H), 5.48 – 5.24 (m, 1H), 5.15 (s, 2H), 5.06 (s, 2H).

$^{13}$C NMR (101 MHz, D6-DMSO) δ 169.92, 137.24, 136.21, 128.85, 128.82, 128.53, 128.39, 128.33, 128.26, 73.88, 66.63, 66.05.

IR (thin film cm$^{-1}$): 696, 739, 751, 972, 1020, 1091, 1221, 1269, 1348, 1454, 1529, 1696, 1754, 3333, 3409.

ESI (M-H$^-$), calc. for 314, found: 314.

HRMS, ESI (M+Na$^+$), calc. for (C$_{17}$H$_{17}$NO$_3$Na) 338.1005, found: 338.1007.

m.p. 107.1-109.0 °C.

![Reactions](image)
Compound was prepared from benzamide (121 mg, 1.0 mmol) and 2-oxo-2-phenylacetaldehyde (134 mg, 1.0 mmol) in diethyl ether 3 mL with the general procedure during 12 hours to give 3 in the yield of 35% as the only product.

$^1$H NMR (400 MHz, DMSO) $\delta$ 9.02 (d, $J = 7.8$ Hz, 2H), 7.94 – 7.90 (m, 3H), 7.62 – 7.29 (m, 12H), 7.05 (t, $J = 7.7$ Hz, 1H).

\[
\begin{align*}
\text{BnO} & \quad \text{CONH}_2 \\
\text{R} & \quad \text{BnO} \\
\quad & \quad \text{CON} \quad \text{OH} \quad \text{CON} \\
\quad & \quad \text{OH} \quad \text{CON} \quad \text{OH}
\end{align*}
\]

Compound 5

1. Compound 5 was prepared from benzamide (121 mg, 1.0 mmol) and 2-(benzyloxy)acetaldehyde (150 mg, 1.0 mmol) in diethyl ether 2.5 mL with the general procedure during 12 hours in the yield of 50% as the only product.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 8.87 (d, $J = 8.8$ Hz, 1H), 7.86 (dd, $J = 12.8$, 5.5 Hz, 2H), 7.57 – 7.38 (m, 3H), 7.38 – 7.22 (m, 5H), 5.79 (dt, $J = 8.6$, 6.0 Hz, 1H), 4.66 – 4.46 (m, 2H), 3.67 (ddd, $J = 42.6$, 10.4, 6.1 Hz, 2H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 166.94, 138.73, 134.58, 131.83, 128.66, 128.57, 128.02, 127.92, 127.86, 77.31, 72.60, 70.90.

\[
\begin{align*}
\text{sp3} & \quad \text{O} \\
\text{sp3} & \quad \text{O} \\
\text{R} & \quad \text{OH} \\
\text{NH} & \quad \text{R}
\end{align*}
\]

Prepare for 7a:

Compound was prepared from benzamide (121 mg, 1.0 mmol) and 6 (130 mg, 1.0 mmol) in diethyl ether 3 mL with the general procedure during 12 hours in the yield of 55% as a mixture of diastereoisomers in the ratio of 1:1.

$^1$H NMR (400 MHz, D6-DMSO) $\delta$ 8.79 (t, $J = 9.9$ Hz, 2H), 7.86 – 7.79 (m, 2H), 7.74 (d, $J = 7.2$ Hz, 2H), 7.55 – 7.35 (m, 7H), 5.68 – 5.59 (m, 1H), 5.44 (t, $J = 8.6$ Hz, 1H), 4.33 (dd, $J = 13.1$, 6.7 Hz, 1H), 4.19 (dd, $J = 12.8$, 6.3 Hz, 1H), 4.11 (dd, $J = 8.5$, 4.8 Hz, 1H), 4.03 (dd, $J = 8.4$, 6.5 Hz, 1H), 3.97 (dd, $J = 8.6$, 6.8 Hz, 1H), 3.68 (dd, $J = 8.8$, 4.9 Hz, 1H), 1.47 (s, 3H), 1.33 – 1.24 (m, 9H).

$^{13}$C NMR (101 MHz, D6-DMSO) $\delta$ 166.41, 135.66, 134.86, 134.50, 134.33, 132.31, 131.63, 129.54, 128.57, 128.41, 128.10, 127.98, 124.55, 109.75, 109.41, 109.16, 101.40, 80.20, 79.84, 77.13, 76.95, 75.99, 70.70, 66.44, 27.03, 26.95, 25.98, 25.77.
IR (thin film cm⁻¹): 693, 1064, 1101, 1150, 1223, 1252, 1370, 1381, 1491, 1530, 1580, 1603, 1649, 1656, 3316.
ESI (M+H⁺), calc. for 252.  found: 252.
HRMS, ESI (M+Na⁺), calc. for (C₁₁H₁₂NO₄Na) 274.1056, found: 274.1059.

Prepare for 7b:
Compound 7b was prepared from 2-phenylacetamide (135 mg, 1 mmol) and 6 (130 mg, 1 mmol) in diethyl ether 3 mL with the general procedure during 12 hours in the yield of 55% as a mixture of diastereoisomers in the ratio of 1:1.

¹H NMR (400 MHz, D6-DMSO) δ 8.51 (d, J = 9.3 Hz, 1H), 8.44 (d, J = 9.6 Hz, 1H), 7.39 (d, ylacetamide2, 1370, dd, J = 9.5, 7.1 Hz, 1H), 5.16 (dd, J = 9.1, 7.8 Hz, 1H), 4.08 (dd, J = 12.6, 6.9 Hz, 1H), 4.00 (dd, J = 12.3, 6.3 Hz, 1H), 3.94 (t, J = 7.3 Hz, 1H), 3.86 (dt, J = 8.3, 5.5 Hz, 2H), 3.58 (t, medium2, 1370, 1381, 1491, 1530, 1580, 1603, 1649, 1656, 3316..10.
³C NMR (101 MHz, D6-DMSO) δ 171.20, 170.44, 136.52, 136.38, 129.81, 129.56, 128.62, 128.47, 126.83, 126.66, 109.68, 109.19, 79.07, 77.03, 75.95, 66.23, 65.32, 42.68, 42.59, 26.84, 26.8, 25.87, 25.74.
IR(thin film cm⁻¹): 1069, 1083, 1105, 1215, 1370, 1385, 1453, 1497, 1546, 1660, 3281.
ESI (M+H⁺), calc. for 266.  found: 266.
HRMS, ESI (M+Na⁺), calc. for (C₁₄H₁₉NO₄Na) 288.1212, found: 288.1208.

Prepare for 7c:
Compound 7c was prepared from cinnamamide (147 mg, 1.0 mmol) and 6 (130 mg, 1.0 mmol) in diethyl ether 3 mL with the general procedure during 12 hours in the yield of 58% as a mixture of diastereoisomers in the ratio of 1:1.

¹H NMR (400 MHz, D6-DMSO) (400 MHz, 5J = 9.5 Hz, 2H), 7.65 as the only product.edudd, J = 32.8, 15.8 Hz, 2H), 5.51 (dd, J = 9.4, 7.3 Hz, 1H), 5.38 1 (dd, pro 1H), 4.27 – 4.11 (m, 1H), 4.12 – 3.88 (m, 4H), 3.68 (dd, J = 8.7, 5.1 Hz, 1H), 1.45 (s, 3H), 1.35 , 4.27 – 4.11 ( 
³C NMR (101 MHz, D6-DMSO) δ 165.73, 164.97, 140.38, 139.92, 135.12, 130.10, 129.41, 128.04, 122.64, 122.08, 109.77, 109.28, 79.27, 78.85, 77.18, 76.10, 66.32, 65.49, 26.90, 26.82, 25.88, 25.77.
ESI (M+H⁺), calc. for 266.  found: 266.
HRMS, ESI (M+Na⁺), calc. for (C₁₄H₁₉NO₄Na) 288.1212, found: 288.1208.

```
\[
\begin{align*}
\text{SO}_2\text{NH}_2 + \text{HOOC-COEt} & \xrightarrow{5 \text{ mol\% (PHO}_2\text{POOH)}} \text{ether, r.t. 12 h} \rightarrow \text{SO}_2\text{NH-CON} & \text{COEt} \\
\end{align*}
\]
```

Compound was prepared from p-toluenesulfonamide (171 mg, 1.0 mmol) and ethyl glyoxalate (50% in toluene, 198 µl, 1.0 mmol in diethyl ether 5 mL with the general procedure during 12 hours to give 10 in the yield of 65% as the only product.

¹H NMR (400 MHz, D6-DMSO) δ 8.83 (d, J = 9.2 Hz, 1H), 7.71 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 6.67 (d, J = 6.9 Hz, 1H), 5.10 (dd, J = 9.1, 6.9 Hz, 1H), 4.12 – 3.92 (m, 2H), 2.38 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H).
\(^{13}\)C NMR (101 MHz, D6-DMSO) \(\delta\) 169.16, 142.84, 140.03, 129.66, 126.91, 75.95, 61.40, 21.40, 14.26.

IR (thin film cm\(^{-1}\)): 673, 811, 1070, 1087, 1104, 1158, 1232, 1305, 1355, 1743, 3280, 3359.

ESI (M+H\(^{+}\)), calc. for 260, found: 260.

HRMS, ESI (M+Na\(^{+}\)), calc. for (C\(_{16}\)H\(_{13}\)NO\(_{5}\)Na) 282.0412, found: 282.0416.

m.p. 112.7-115.1 °C.

Scale up:

![Chemical Structure](image)

Ethyl 2-(((benzloyx)carbonyl)amino)-2-hydroxyacetate

Compound was prepared from Cbz-NH\(_2\) (15.9 g, 100 mmol) and ethyl glyoxalate (50% in toluene, 19.8 mL, 100 mmol) in diethyl ether 300 mL with the general procedure during 20 hours in the yield of 81%(20.5 g).
NMR Spectra