Supplementary Information

Synthesis of Oxime Ethers via A Formal Reductive O–H Bond Insertion of Oximes to α-Keto Esters

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I. General Information

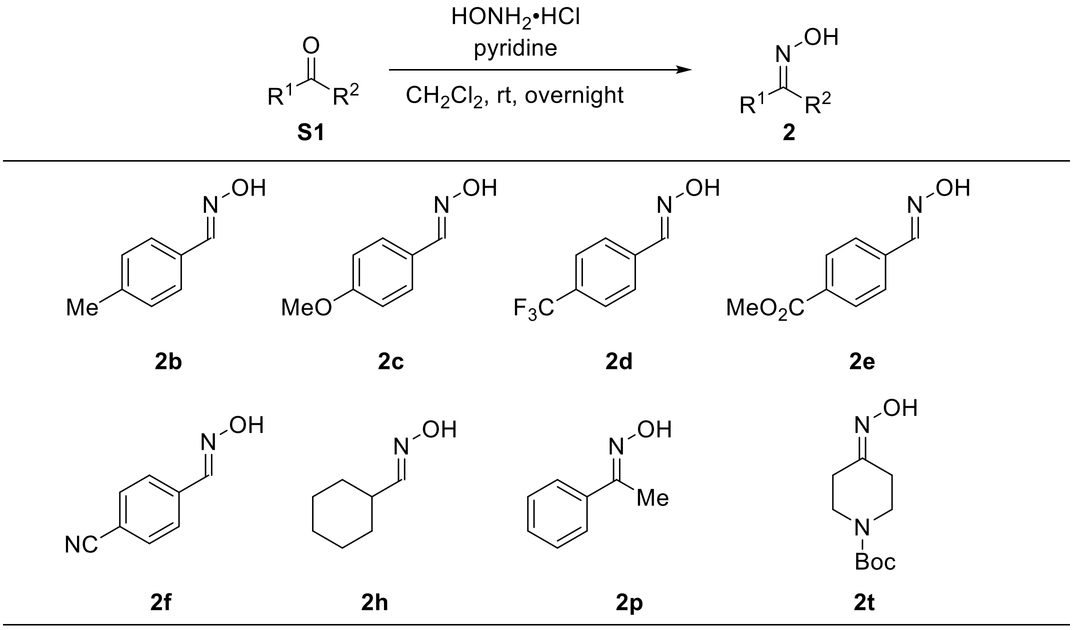
All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Flash column chromatography was performed using Silicycle silica gel (SiliaFlash® F60, 40-63 μm) or Biotage Automated Liquid Chromatography System Isolera One using Biotage SNAP KP-Sil 10g or 25g silica gel cartridges. Preparative thin-layer chromatography (preparative TLC) separations were carried out on 0.50 mm E. Merck silica gel plates (60 F_{254}). ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECZ400S, a Varian VNS AS 500 MHz or a Bruker AVANCE III HD 600 MHz operating at 400 MHz/101 MHz, 500 MHz/126 MHz, or 600 MHz/150 MHz for ^{1}H and ^{13}C acquisitions, respectively. Chemical shifts are reported in ppm with the solvent resonance or TMS as the internal standard. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), ddd (doublet of doublet of doublets), AB q (AB quartet), m (multiplet) and br (broad). Infrared (IR) spectra were recorded on a Perkin-Elmer SpectrumOne A spectrometer using NaCl plates or KBr pallets. High-resolution mass spectra (HRMS) were conducted on an FT-ESI mass analyzer. Melting points (uncorrected) were determined on BÜCHI M-565 apparatus.

II. Experimental Section

The α-keto esters **1b**,[1] **1h**,[2] **1i**,[2] and **1k**[1] were prepared according to literatures. The spectra data of these known compounds were identical with those reported in the literatures, respectively.

[1] M. Hayashi, S. Nakamura, *Angew. Chem. Int. Ed.*, **2011**, *50*, 2249-2252.
[2] R. Xie, C. Liu, R. Lin, R. Zhang, H. Huang, M. Chang, *Org. Lett.*, **2022**, *24*, 5646-5650.

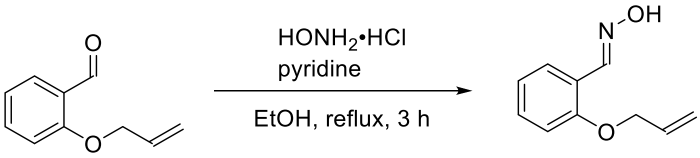
General procedure for the preparation of oximes 2 (method A)



To a solution of aldehyde or ketone **S1** (10 mmol) in CH_2Cl_2 (30 mL) were added hydroxylamine·HCl (1.4 g, 20 mmol) and pyridine (1.6 mL, 20 mmol) at 0 °C. After being stirred at room temperature for 24 h, the reaction mixture was diluted with AcOEt (200 mL). The mixture was washed with 1 M HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography to give oximes **2**. Analytical data of **2b**,[1,3] **2c**,[3] **2d**,[3] **2e**,[1] **2f**,[3] **2h**,[3] **2p**,[1] and **2t**[1] are in accordance with literature data.

[1] M. Hayashi, S. Nakamura, *Angew. Chem. Int. Ed.*, **2011**, *50*, 2249-2252.
[3] S. Minakata, S. Okumura, T. Nagamachi, Y. Takeda, *Org. Lett.*, **2011**, *13*, 2966-2969.

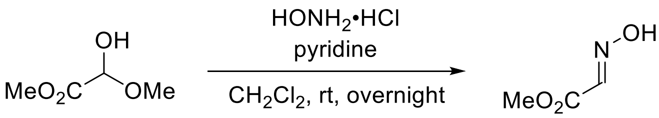
(*E*)-2-(2-Propen-1-yloxy)benzaldehyde oxime (2g)



S2 **2g**

To a solution of 2-allyloxybenzaldehyde (**S2)** (2.98 mL, 20 mmol) in EtOH (20 mL) were added hydroxylamine·HCl (2.08 g, 30 mmol) and pyridine (1.93 mL, 24 mmol) at room temperature. After being stirred at reflux for 3 h, the reaction mixture was diluted with AcOEt (300 mL). The mixture was washed with 1 M HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 5/1-2/1) to give oxime **2g** (3.32 g, 94% yield) as a yellow oil. IR (neat) ν_{max} 3284 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.65 (br s, 1H), 8.57 (s, 1H), 7.70 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.32-7.28 (m, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.08-5.98 (m, 1H), 5.42-5.26 (m, 2H), 4.56 (d, *J* = 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 156.5, 146.4, 132.8, 131.1, 126.8, 120.9, 120.7, 117.6, 112.4, 69.1; HRMS (ESI) *m/z*: $[M +H]^+$ Calcd for $C_{10}H_{12}O_2N$ 178.0863; Found 178.0864.

Methyl (2*E*)-2-(hydroxyimino)acetate (2i)

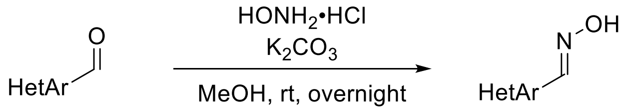


S3 **2i**

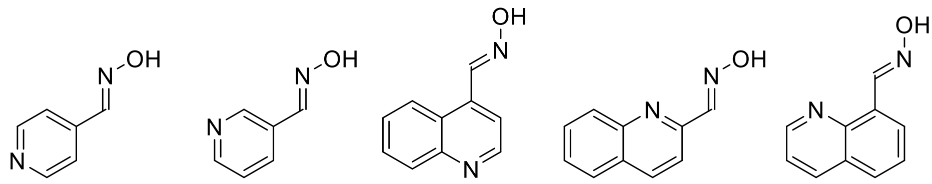
To a solution of methyl 2-hydroxy-2-methoxyacetate (**S3)** (1.2 g, 10 mmol) in CH_2Cl_2 (50 mL) were added hydroxylamine·HCl (1.4 g, 20 mmol) and pyridine (3.24 mL, 40 mmol) at 0 °C. After being stirred at room temperature for 24 h, the reaction mixture was diluted with AcOEt (300 mL). The mixture was washed with 1 M HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 5/1-2/1) to give oximes **2i** (509.0 mg, 49% yield) as a white solid. Analytical data are in accordance with literature data.[4]

[4] D. J. Ritson, R. J. Cox, J. Berge, *Org. Biomol. Chem.*, **2004**, *2*, 1921-1933.

General procedure for the preparation of heteroarylaldoximes 2 (method B)



S4 → **2**



2j **2k**[a] **2m** **2n** **2o**

a) Reaction was carried out at reflux.

To a solution of aldehyde **S4** (10 mmol) in MeOH (30 mL) were added hydroxylamine·HCl (1.4 g, 20 mmol) and K_2CO_3 (2.16 g, 20 mmol) at room temperature. After being stirred at room temperature for 24 h, the reaction mixture was diluted with AcOEt (200 mL). The mixture was washed with H_2O (x2) and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography to give oximes **2**. Analytical data of **2j**,[5] **2k**,[6] **2n**,[5,7] and **2o**[8] are in accordance with literature data.

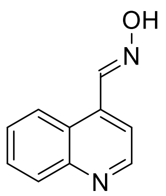
[5] J. Yu, Y. Jin, M. Lu, *Adv. Synth. Catal.*, **2015**, *357*, 1175-1180.

[6] J. K. Augustine, R. Kumar, A. Bombrun, A. B. Mandal, *Tetrahedron Lett.*, **2011**, *52*, 1074-1077.

[7] X. Gao, F. Zhang, G. Deng, L. Yang, *Org. Lett.*, **2014**, *16*, 3664-3667.

[8] D. X. Ngo, W. W. Kramer, B. J. McNicholas, H. B. Gray, B. J. Brennan, *Inorg. Chem.*, **2019**, *58*, 737-746.

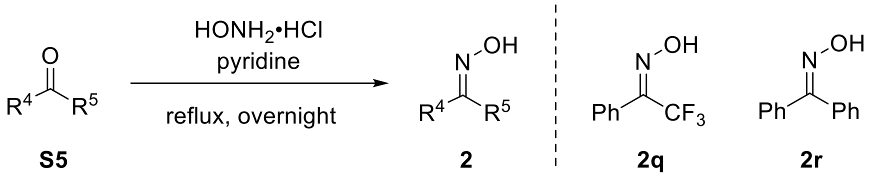
(*E*)-4-Quinolinecarboxaldehyde oxime (2m)



To a solution of 4-quinoline carboxaldehyde (471.5 mg, 3.0 mmol) in MeOH (10 mL) were added hydroxylamine·HCl (416.9 mg, 6.0 mmol) and K_2CO_3 (829.3 mg, 6.0 mmol) at room temperature. After being stirred at room temperature for 24 h, the reaction mixture was diluted with AcOEt (200 mL). The mixture was washed with H_2O (x2) and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 1/2) to give oxime **2m** (469.8 mg, 91%) as a white solid. Mp 179-180 °C; IR (KBr) ν_{max} 3160 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ 8.82 (d, *J* = 4.6 Hz, 1H), 8.75 (s, 1H), 8.61-8.58 (m, 1H), 8.07-8.04 (m, 1H), 7.80-7.73 (m, 2H), 7.67-7.62 (m, 1H); ^{13}C-NMR (101 MHz, CD_3OD) δ 150.8, 149.3, 147.1, 139.6, 131.1, 129.8, 128.7, 126.7, 126.0, 120.6.; HRMS (ESI) *m*/*z*:

[M + H]+ Calcd for $C_{10}H_9ON_2$ 173.0709; Found 173.0708.

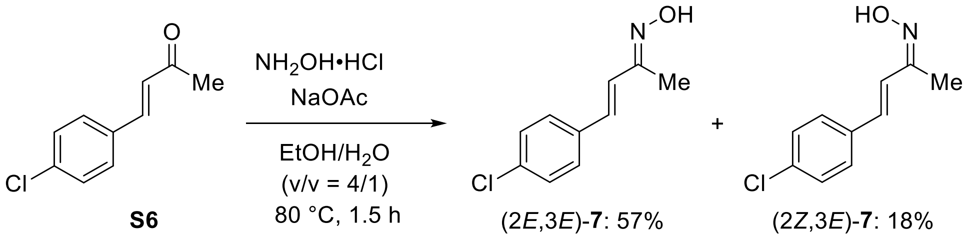
General procedure for the preparation of oximes 2 (method C)



To a solution of ketone **S5** (20 mmol) in pyridine (20 mL) was added hydroxylamine·HCl (2.08 g, 30 mmol) at room temperature. After being stirred at reflux for 24 h, the reaction mixture was diluted with AcOEt (300 mL). The mixture was washed with 1 M HCl (x2), saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 1/2) to give oximes **2q** and **2r**. Analytical data of **2q**[9] and **2r**[1] are in accordance with literature data.

[1] M. Hayashi, S. Nakamura, *Angew. Chem. Int. Ed.*, **2011**, *50*, 2249-2252.
[9] I. Protasova, B. Bulat, N. Jung, S. Bräse, *Org. Lett.*, **2017**, *19*, 34-37.

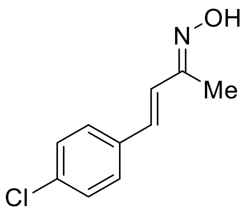
(2*E*,3*E*)-4-(4-Chlorophenyl)-3-buten-2-one oxime ((2*E*,3*E*)-7) and (2*Z*,3*E*)-4-(4-Chlorophenyl)-3-buten-2-one oxime ((2*Z*,3*E*)-7)



To a solution of hydroxylamine·HCl (494.7 mg, 6.4 mmol) in EtOH (8.0 mL) and H_2O (2.0 mL) was added AcONa (616.0 mg, 8.0 mmol) at room temperature. After being stirred at reflux for 30 min, ketone **S6**[10] (722.5 mg, 4.0 mmol) was added. The reaction mixture was stirred for 1 h, diluted with AcOEt (100 mL). The mixture was washed with 1 M HCl, saturated $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 2/1) to give oximes (2*E*,3*E*)-**7**[11] (446.5 mg, 57%) and (2*Z*,3*E*)-**7** (143.4 mg, 18%).

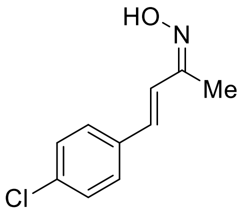
[10] Wang, J.; Li, J.; Wang, Y.; He, S.; You, H.; Chen, F.-E., *ACS Catal.* **2022**, *12*, 9629–9637.
[11] Stivanin, M. L.; Duarte, M.; Leão, L. P. M. O.; Saito, F. A.; Jurberg, I. D., *J. Org. Chem.*, **2021**, *86*, 17528–17532.

(2*E*,3*E*)-4-(4-Chlorophenyl)-3-buten-2-one oxime ((2*E*,3*E*)-7) [11]



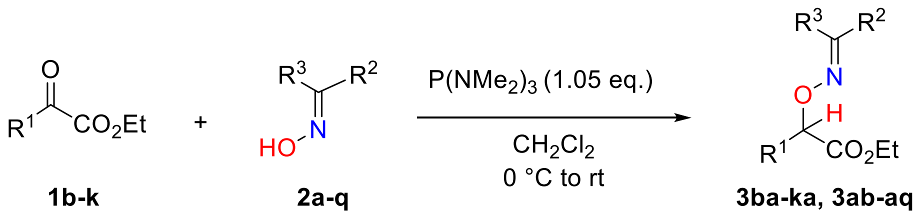
(2*E*,3*E*)-**7**; A white solid; Mp 125-126 °C;IR (KBr) ν_{max} 3194 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.33-7.30 (m, 2H), 6.85 (d, J = 16.5 Hz, 1H), 6.81 (d, J = 16.5 Hz, 1H), 2.14 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 156.6, 134.8, 134.1, 132.1, 128.9, 128.0, 126.3, 9.7; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{10}H_{11}ON^{35}Cl$ 196.0524; Found 196.0525.

(2*Z*,3*E*)-4-(4-Chlorophenyl)-3-buten-2-one oxime ((2*Z*,3*E*)-7)



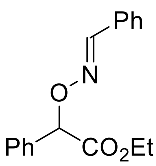
(2*Z*,3*E*)-**7**; A white solid; Mp 132-133 °C; IR (KBr) ν_{max} 3152 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 16.9 Hz, 1H), 7.48-7.45 (m, 2H), 7.35-7.32 (m, 2H), 6.89 (d, J = 16.5 Hz, 1H), 2.14 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.1, 135.1, 134.8, 134.7, 129.0, 128.6, 117.2, 16.8; HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{10}H_{11}ON^{35}Cl$ 196.0524; Found 196.0525.

General procedure for a formal reductive O−H bond insertion reaction of α-keto esters 1 with oximes 2



To a solution of α-keto ester **1** (0.25 mmol) and oxime **2** (0.26 mmol) in CH_2Cl_2 (2.5 mL) was slowly added tris(dimethylamino)phosphine (47.3 μL, 0.26 mmol) at 0 °C under an argon atmosphere. After being stirred at the same temperature for 5 min, the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with $CHCl_3$ (5 mL), and concentrated under reduced pressure. The residue was purified by flash column chromatography (Biotage Isolera One) or preparative TLC to afford oxime ethers **3**.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]benzeneacetate (3aa)

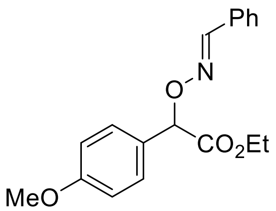


α-Keto ester **1a** (39.7 μL, 0.25 mmol) and oxime **2a** (28.4 μL, 0.26 mmol) were used. 46.0 mg, 78% yield. Purification by preparative TLC (hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1752 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.59-7.51 (m, 4H), 7.41-7.34 (m, 6H), 5.71 (s, 1H), 4.28-4.18 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C-NMR (151 MHz, $CDCl_3$) δ 170.5, 150.6, 134.8, 131.7, 130.2, 129.0, 128.6, 127.7, 127.3, 83.8, 61.2, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{17}O_3NNa$ 306.1104; Found 306.1105.

A formal reductive O-H bond insertion reaction of oxime 2a with α-keto ester 1a on 10.0 mmol scale (Gram-scale synthesis)

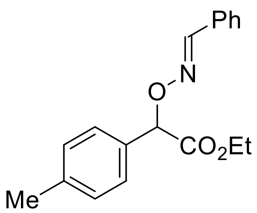
To a solution of ethyl benzoylformate (**1a**) (1.59 mL, 10.0 mmol) and α-benzaldoxime (**2a**) (1.17 mL, 10.5 mmol) in CH_2Cl_2 (100 mL) was slowly added tris(dimethylamino)phosphine (1.91 mL, 10.5 mmol) at 0 °C under an argon atmosphere. After being stirred at the same temperature for 5 min, the reaction mixture was allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt = 10/1 to 5/1) to afford oxime ether **3aa** (2.37 g, 84% yield) as a colorless oil.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-methoxybenzeneacetate (3ba)



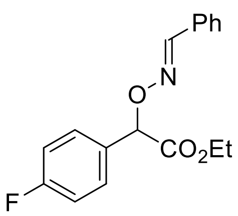
α-Keto ester **1b** (45.4 μL, 0.25 mmol) was used. 61.6 mg, 79% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.59-7.56 (m, 2H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.38-7.35 (m, 3H), 6.92 (d, *J* = 9.1 Hz, 2H), 5.64 (s, 1H), 4.28-4.18 (m, 2H), 3.82 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.8, 160.2, 150.4, 131.7, 130.1, 129.2, 128.6, 127.3, 126.9, 114.1, 83.3, 61.2, 55.3, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_4NNa$ 336.1206; Found 336.1205.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-methylbenzeneacetate (3ca)



α-Keto ester **1c** (44.1 μL, 0.25 mmol) was used. 60.0 mg, 81% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1747 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.60-7.56 (m, 2H), 7.42-7.33 (m, 5H), 7.20 (d, *J* = 7.8 Hz, 2H), 5.67 (s, 1H), 4.30-4.16 (m, 2H), 2.36 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.7, 150.5, 139.0, 131.8, 131.7, 130.1, 129.4, 128.6, 127.7, 127.3, 83.6, 61.2, 21.2, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_3NNa$ 320.1257; Found 320.1255.

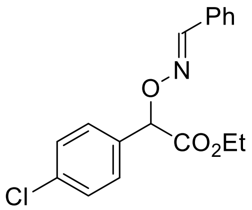
Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-fluorobenzeneacetate (3da)



α-Keto ester **1d** (40.9 μL, 0.25 mmol) was used. 49.0 mg, 65% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.59-7.49 (m, 4H), 7.42-7.34 (m, 3H), 7.12-7.05 (m, 2H), 5.68 (s, 1H), 4.30-4.17 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$) δ 170.3, 164.1 (C-F, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 162.1 (C-F, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 150.7, 131.6, 131.2, 130.78 (C-F, $^{4}J_{C\text{-}F}$ = 2.0

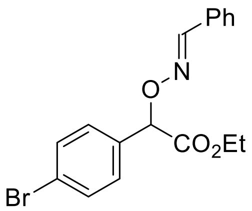
Hz), 130.77 (C-F, $^4J_{C\text{-}F}$ = 2.0 Hz), 130.3, 129.6 (C-F, $^3J_{C\text{-}F}$ = 8.5 Hz), 129.5 (C-F, $^3J_{C\text{-}F}$ = 8.5 Hz), 128.7, 127.4, 115.7 (C-F, $^2J_{C\text{-}F}$ = 21.0 Hz), 115.5 (C-F, $^2J_{C\text{-}F}$ = 21.0 Hz), 83.0, 61.4, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{16}O_3NFNa$ 324.1006; Found 324.1003.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-chlorobenzeneacetate (3ea)



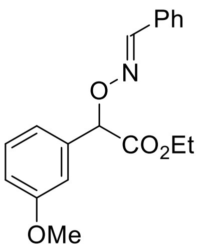
α-Keto ester **1e** (53.2 mg, 0.25 mmol) was used. 54.8 mg, 69% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.57 (dd, *J* = 7.3, 2.3 Hz, 2H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.38-7.36 (m, 5H), 5.67 (s, 1H), 4.28-4.18 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.1, 150.8, 134.9, 133.4, 131.5, 130.3, 129.0, 128.9, 128.7, 127.4, 82.9, 61.5, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{16}O_3N^{35}Cl\,Na$ 340.0711; Found 340.0711.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-bromobenzeneacetate (3fa)



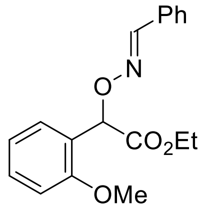
α-Keto ester **1f** (43.4 μL, 0.25 mmol) was used. 58.1 mg, 64% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.58-7.52 (m, 4H), 7.42-7.34 (m, 5H), 5.65 (s, 1H), 4.27-4.18 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.0, 150.8, 133.9, 131.8, 131.4, 130.3, 129.3, 128.7, 127.4, 123.2, 83.0, 61.5, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{16}O_3N^{79}BrNa$ 384.0206; Found 384.0209.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-3-methoxybenzeneacetate (3ha)



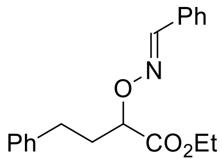
α-Keto ester **1h** (52.1 mg, 0.25 mmol) was used. 64.8 mg, 83% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A yellow oil; IR (neat) ν_{max} 1752 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.59-7.57 (m, 2H), 7.39-7.29 (m, 4H), 7.12-7.07 (m, 2H), 6.92 (dd, *J* = 7.8, 2.7 Hz, 1H), 5.68 (s, 1H), 4.29-4.19 (m, 2H), 3.83 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.4, 159.7, 150.6, 136.1, 131.6, 130.2, 129.7, 128.6, 127.3, 120.0, 114.9, 112.8, 83.6, 61.3, 55.3, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_4NNa$ 336.1206; Found 336.1200.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-2-methoxybenzeneacetate (3ia)



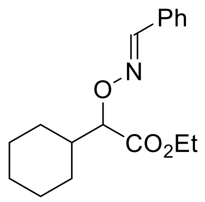
α-Keto ester **1i** (52.1 mg, 0.25 mmol) was used. 59.9 mg, 77% yield. Purification by preparative TLC (hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.59-7.57 (m, 2H), 7.46 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.39-7.33 (m, 4H), 7.01-6.93 (m, 2H), 6.14 (s, 1H), 4.28-4.22 (m, 2H), 3.88 (s, 3H), 1.25 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.0, 157.3, 150.1, 131.8, 130.4, 130.0, 129.2, 128.6, 127.3, 123.4, 120.7, 111.1, 78.0, 61.1, 55.7, 14.2; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{18}H_{19}O_4NNa$ 336.1206; Found 336.1210.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-4-phenylbutanoate (3ja)



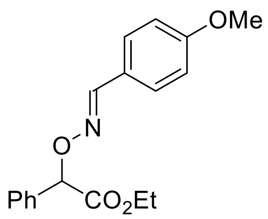
α-Keto ester **1j** (47.3 μL, 0.25 mmol) was used. 40.7 mg, 52% yield. Purification by preparative TLC (hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1743 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.59-7.57 (m, 2H), 7.38-7.19 (m, 8H), 4.73 (t, *J* = 6.6 Hz, 1H), 4.27-4.19 (m, 2H), 2.88-2.77 (m, 2H), 2.23-2.17 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 172.1, 150.0, 141.0, 131.8, 130.1, 128.7, 128.5, 128.4, 127.3, 126.1, 80.9, 61.0, 33.0, 31.4, 14.3; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{19}H_{21}O_3NNa$ 334.1414; Found 334.1412.

Ethyl α-[[(*E*)-(phenylmethylene)amino]oxy]-2-cyclohexylacetate (3ka)



The reaction of α-keto ester **1k** (92.1 mg, 0.50 mmol) and oxime **2a** (56.8 μL, 0.53 mmol) with tris(dimethylamino)phosphine (94.6 μL, 0.53 mmol) at reflux for 3 h gave **3ka** (90.1 mg, 62% yield). Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1743 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.57-7.55 (m, 2H), 7.39-7.34 (m, 3H), 4.52 (d, *J* = 6.4 Hz, 1H), 4.28-4.20 (m, 2H), 1.90-1.59 (m, 7H), 1.38-1.16 (m, 7H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.9, 149.7, 131.9, 130.0, 128.6, 127.2, 86.4, 60.7, 39.8, 28.9, 28.5, 26.1, 26.0, 25.9, 14.3; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{17}H_{23}O_3NNa$ 312.1570; Found 312.1570.

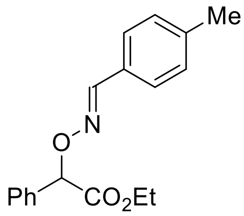
Ethyl α-[[(*E*)-[(4-methoxyphenyl)methylene]amino]oxy]benzeneacetate (3ab)



Oxime **2b** (34.3 mg, 0.26 mmol) was used. 59.2 mg, 76% yield. Purification by preparative TLC (hexane/AcOEt = 1/1); A colorless oil; IR (neat) ν_{max} 1747 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.54-7.50 (m, 4H), 7.42-7.36 (m, 3H), 6.90-6.86 (m, 2H), 5.68 (s, 1H), 4.26-4.20 (m, 2H), 3.82 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101

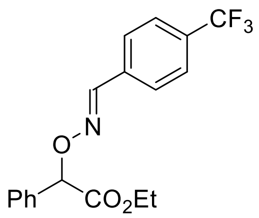
MHz, $CDCl_3$) δ 170.7, 161.2, 150.2, 134.9, 128.94, 128.85, 128.6, 127.7, 124.2, 114.1, 83.6, 61.2, 55.3, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_4NNa$ 336.1206; Found 336.1203.

Ethyl α-[[(*E*)-[(4-methylphenyl)methylene]amino]oxy]benzeneacetate (3ac)



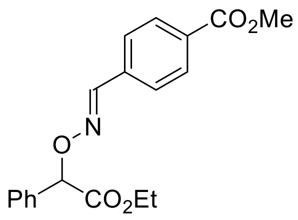
Oxime **2c** (35.1 mg, 0.26 mmol) was used. 57.6 mg, 78% yield. Purification by preparative TLC (hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.54-7.46 (m, 4H), 7.42-7.34 (m, 3H), 7.17 (d, *J* = 7.8 Hz, 2H), 5.69 (s, 1H), 4.29-4.16 (m, 2H), 2.35 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.6, 150.6, 140.4, 134.8, 129.4, 129.0, 128.8, 128.6, 127.7, 127.3, 83.7, 61.2, 21.5, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_3NNa$ 320.1257; Found 320.1255.

Ethyl α-[[(*E*)-[[(4-trifluoromethyl)phenyl]methylene]amino]oxy]benzeneacetate (3ad)



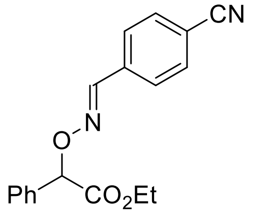
Oxime **2d** (49.2 mg, 0.26 mmol) was used. 63.1 mg, 72% yield. Purification by preparative TLC (hexane/Et_2O = 5/1); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.54-7.50 (m, 2H), 7.44-7.38 (m, 3H), 5.73 (s, 1H), 4.29-4.17 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H);^{13}C-NMR (126 MHz, $CDCl_3$) δ 170.3, 149.1, 135.1, 134.5, 132.2 (C-F, $^2J_{C-F}$ = 32.3 Hz), 131.9 (C-F, $^2J_{C-F}$ = 32.3 Hz), 131.7 (C-F, $^2J_{C-F}$ = 32.3 Hz), 131.4 (C-F, $^2J_{C-F}$ = 32.3 Hz), 129.2, 128.7, 127.7, 127.5, 127.1 (C-F, $^1J_{C-F}$ = 271.3 Hz), 125.68 (C-F, $^3J_{C-F}$ = 3.8 Hz), 125.65 (C-F, $^3J_{C-F}$ = 3.8 Hz), 125.62 (C-F, $^3J_{C-F}$ = 3.8 Hz), 125.59 (C-F, $^3J_{C-F}$ = 3.8 Hz), 124.9 (C-F, $^1J_{C-F}$ = 271.3 Hz), 122.7 (C-F, $^1J_{C-F}$ = 271.3 Hz), 120.6 (C-F, $^1J_{C-F}$ = 271.3 Hz), 84.0, 61.4, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{16}O_3NF_3$ 374.0975; Found 374.0973.

Ethyl α-[[(*E*)-[[(4-methoxycarbonyl)phenyl]methylene]amino]oxy]benzeneacetate (3ae)



Oxime **2e** (46.6 mg, 0.26 mmol) was used. 75.3 mg, 88% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A white solid; Mp 99-100 °C; IR (KBr) ν_{max} 1745, 1716 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.44-7.39 (m, 3H), 5.73 (s, 1H), 4.31-4.17 (m, 2H), 3.93 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.3, 166.5, 149.6, 135.8, 134.4, 131.3, 129.9, 129.1, 128.7, 127.7, 127.2, 83.9, 61.4, 52.3, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{19}O_5NNa$ 364.1155; Found 364.1152.

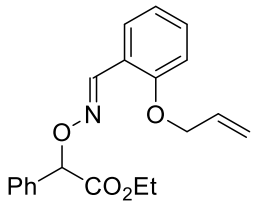
Ethyl α-[[(*E*)-[(4-cyanophenyl)methylene]amino]oxy]benzeneacetate (3af)



Oxime **2f** (38.0 mg, 0.26 mmol) was used. 61.3 mg, 80% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A white solid; Mp 117-118 °C; IR (KBr) ν_{max} 2223, 1752 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.72-7.64 (m, 4H), 7.54-7.49 (m, 2H), 7.44-7.37 (m, 3H), 5.72 (s, 1H), 4.31-4.17 (m, 2H), 1.25 (t, *J* = 7.3 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.2, 148.7, 135.9, 134.3, 132.4, 129.3, 128.8, 127.7, 118.4, 113.4, 84.1, 61.5, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{16}O_3N_2Na$ 331.1053; Found 331.1049.

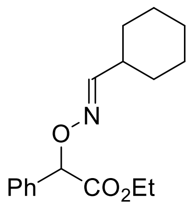
One of carbons (C*sp*^{2}) overlapped with other carbons (C*sp*^{2}) in ^{13}C NMR spectrum.

Ethyl α-[[(*E*)-[[2-(2-propen-1-yloxy)phenyl]methylene]amino]oxy]benzeneacetate (3ag)



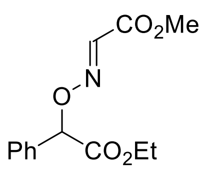
Oxime **2g** (46.1 mg, 0.26 mmol) was used. 50.9 mg, 60% yield. Purification by preparative TLC (hexane/Et_2O = 2/1); A white solid; Mp 86-87 °C; IR (KBr) ν_{max} 1742 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.78 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.55-7.52 (m, 2H), 7.42-7.29 (m, 4H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.07-5.98 (m, 1H), 5.70 (s, 1H), 5.40 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.28 (dq, *J* = 10.5, 1.4 Hz, 1H), 4.55 (td, *J* = 3.4, 1.7 Hz, 2H), 4.27-4.19 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.7, 156.7, 146.7, 134.9, 132.8, 131.4, 128.9, 128.6, 127.7, 126.6, 120.8, 120.5, 117.8, 112.3, 83.7, 69.1, 61.2, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{21}O_4NNa$ 362.1363; Found 362.1358.

Ethyl α-[[(*E*)-(cyclohexylmethylene)amino]oxy]benzeneacetate (3ah)



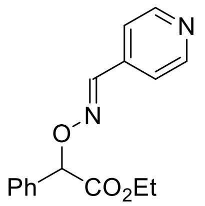
Oxime **2h** (33.1 mg, 0.26 mmol) was used. 27.9 mg, 39% yield. Purification by preparative TLC (hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1747 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H), 7.39-7.34 (m, 3H), 5.53 (s, 1H), 4.25-4.16 (m, 2H), 2.27-2.21 (m, 1H), 1.80-1.59 (m, 6H), 1.31-1.17 (m, 7H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.7, 157.0, 135.0, 128.8, 128.6, 127.6, 83.0, 61.1, 38.4, 30.2, 25.8, 25.3, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{17}H_{23}O_3NNa$ 312.1570; Found 312.1569.

Ethyl α-[[(*E*)-(2-methoxy-2-oxoethylidene)amino]oxy]benzeneacetate (3ai)



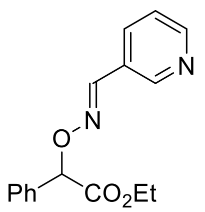
Oxime **2i** (26.8 mg, 0.26 mmol) was used. 47.3 mg, 71% yield. Purification by preparative TLC ($CHCl_3$); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.47-7.38 (m, 5H), 5.79 (s, 1H), 4.27-4.16 (m, 2H), 3.86 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 169.4, 161.9, 142.3, 133.7, 129.4, 128.8, 127.8, 84.8, 61.6, 52.6, 14.0; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{15}O_5NNa$ 288.0842; Found 288.0841.

Ethyl α-[[(*E*)-(4-pyridinylmethylene)amino]oxy]benzeneacetate (3aj)



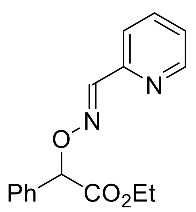
Oxime **2j** (31.8 mg, 0.26 mmol) was used. 57.2 mg, 80% yield. Purification by preparative TLC (hexane/AcOEt = 1/2); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.64 (d, J = 5.9 Hz, 2H), 8.21 (s, 1H), 7.53-7.39 (m, 7H), 5.73 (s, 1H), 4.31-4.17 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.1, 150.3, 148.4, 139.0, 134.2, 129.2, 128.7, 127.7, 121.2, 84.1, 61.4, 14.1; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{17}O_3N_2$ 285.1234; Found 285.1233.

Ethyl α-[[(*E*)-(3-pyridinylmethylene)amino]oxy]benzeneacetate (3ak)



Oxime **2k** (31.8 mg, 0.26 mmol) was used. 63.3 mg, 89% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 1/1); An orange oil; IR (neat) ν_{max} 1749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.62 (d, J = 3.7 Hz, 1H), 8.28 (s, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.54-7.51 (m, 2H), 7.44-7.32 (m, 4H), 5.72 (s, 1H), 4.31-4.17 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.3, 150.7, 148.6, 147.5, 134.4, 134.0, 129.2, 128.7, 127.9, 127.7, 123.7, 84.0, 61.4, 14.1; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{17}O_3N_2$ 285.1234; Found 285.1233.

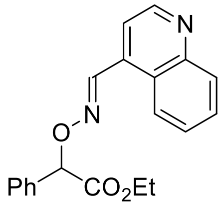
Ethyl α-[[(*E*)-(2-pyridinylmethylene)amino]oxy]benzeneacetate (3al)



Oxime **2l** (31.8 mg, 0.26 mmol) was used. 60.3 mg, 85% yield. Purification by preparative TLC (hexane/AcOEt = 1/2); A yellow oil; IR (neat) ν_{max} 1750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.63-8.62 (m, 1H), 8.35 (s, 1H), 7.79 (d, J = 7.3 Hz, 1H), 7.71-7.67 (m, 1H), 7.55-7.51 (m, 2H), 7.43-7.36 (m, 3H), 7.29-7.26 (m, 1H), 5.77 (s, 1H), 4.30-4.17 (m, 2H), 1.25 (t, J = 6.9 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.3, 151.1, 149.7, 136.4, 134.5, 129.1, 128.7, 127.7, 124.3, 121.4, 84.1, 61.3, 14.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{16}O_3N_2Na$ 307.1053; Found 307.1050.

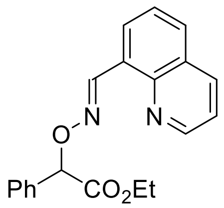
One of carbons (Csp^2) overlapped with other carbons (Csp^2) in ^{13}C NMR spectrum.

Ethyl α-[[(*E*)-(4-quinolinylmethylene)amino]oxy]benzeneacetate (3am)



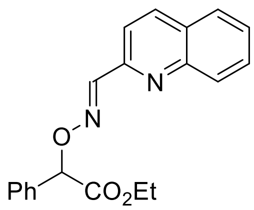
Oxime **2m** (44.8 mg, 0.26 mmol) was used. 66.7 mg, 80% yield. Purification by preparative TLC (hexane/AcOEt = 1/2); A colorless oil; IR (neat) ν_{max} 1748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 4.6 Hz, 1H), 8.87 (s, 1H), 8.38 (d, *J* = 8.7 Hz, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.63-7.55 (m, 4H), 7.46-7.39 (m, 3H), 5.84 (s, 1H), 4.34-4.20 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.2, 150.0, 148.8, 148.0, 135.4, 134.3, 130.2, 129.6, 129.3, 128.8, 127.8, 127.5, 125.1, 124.2, 120.1, 84.2, 61.5, 14.1; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{19}O_3N_2$ 335.1390; Found 335.1388.

Ethyl α-[[(*E*)-(8-quinolinylmethylene)amino]oxy]benzeneacetate (3an)



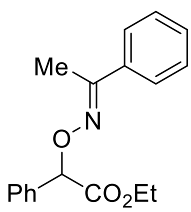
Oxime **2n** (44.8 mg, 0.26 mmol) was used. 64.1 mg, 77% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 2/1); A colorless oil; IR (neat) ν_{max} 1751 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.94-8.91 (m, 1H), 8.25 (d, *J* = 7.3 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.87-7.86 (m, 1H), 7.59-7.53 (m, 3H), 7.44-7.35 (m, 4H), 5.79 (s, 1H), 4.31-4.19 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.7, 150.1, 148.3, 145.9, 136.1, 135.0, 129.8, 129.5, 128.9, 128.6, 128.2, 127.6, 126.5, 126.2, 121.4, 83.8, 61.2, 14.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{18}O_3N_2Na$ 357.1210; Found 357.1206.

Ethyl α-[[(*E*)-(2-quinolinylmethylene)amino]oxy]benzeneacetate (3ao)



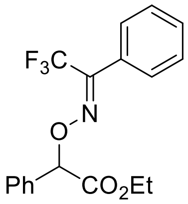
Oxime **2o** (44.8 mg, 0.26 mmol) was used. 66.5 mg, 80% yield. Purification by preparative TLC (hexane/AcOEt = 1/1); A white solid; Mp 66-67 °C; IR (KBr) ν_{max} 1752 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.14-8.08 (m, 2H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.73 (td, *J* = 7.7, 1.2 Hz, 1H), 7.58-7.54 (m, 3H), 7.45-7.37 (m, 3H), 5.80 (s, 1H), 4.32-4.21 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.3, 151.7, 151.5, 147.9, 136.3, 134.4, 129.8, 129.5, 129.1, 128.7, 128.2, 127.7, 127.6, 127.3, 118.2, 84.2, 61.4, 14.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{18}O_3N_2Na$ 357.1210; Found 357.1206.

Ethyl α-[[(*E*)-(1-phenylethylidene)amino]oxy]benzeneacetate (3ap)



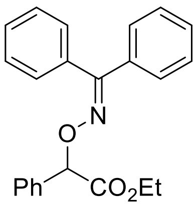
Oxime **2p** (35.1 mg, 0.26 mmol) was used. 52.0 mg, 70% yield. Purification by preparative TLC (hexane/AcOEt = 3/1); A colorless oil; IR (neat) ν_{max} 1749 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66-7.62 (m, 2H), 7.56-7.53 (m, 2H), 7.43-7.33 (m, 6H), 5.72 (s, 1H), 4.27-4.15 (m, 2H), 2.37 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.8, 156.8, 136.1, 135.2, 129.3, 128.8, 128.6, 128.3, 127.6, 126.3, 83.6, 61.1, 14.1, 13.2; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}O_3NNa$ 320.1257; Found 320.1256.

Ethyl α-[[(*E*)-(2,2,2-trifluoro-1-phenylethylidene)amino]oxy]benzeneacetate (3aq)



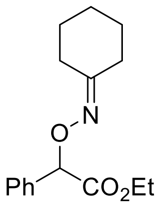
Oxime **2q** (49.2 mg, 0.26 mmol) was used. 72.6 mg, 83% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A colorless oil; IR (neat) ν_{max} 1750 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 2H), 7.47-7.43 (m, 3H), 7.37-7.31 (m, 5H), 5.75 (s, 1H), 4.25-4.20 (m, 2H), 1.25 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$) δ 169.6, 148.3, (C-F, $^2J_{C-F}$ = 32.3 Hz), 148.1 (C-F, $^2J_{C-F}$ = 32.3 Hz), 147.8 (C-F, $^2J_{C-F}$ = 32.3 Hz), 147.5 (C-F, $^2J_{C-F}$ = 32.3 Hz), 133.7, 130.5, 129.2, 128.8, 128.6, 128.4, 127.5, 126.5, 123.7 (C-F, $^1J_{C-F}$ = 273.3 Hz), 121.5 (C-F, $^1J_{C-F}$ = 273.3 Hz), 119.3 (C-F, $^1J_{C-F}$ = 273.3 Hz), 117.1 (C-F, $^1J_{C-F}$ = 273.3 Hz), 85.0, 61.5, 14.0; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{16}O_3NF_3Na$ 374.0975; Found 374.0969.

Ethyl α-[[(diphenylmethylene)amino]oxy]benzeneacetate (3ar)



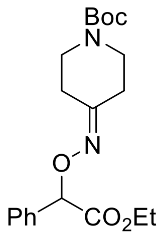
Oxime **2r** (51.3 mg, 0.26 mmol) was used. 84.8 mg, 94% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A white solid; Mp 98-99 °C; IR (KBr) ν_{max} 1744 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56-7.25 (m, 15H), 5.78 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.8, 158.6, 136.2, 134.9, 132.9, 129.7, 129.5, 129.0, 128.6, 128.44, 128.35, 128.2, 127.9, 127.3, 84.0, 61.1, 14.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{21}O_3NNa$ 382.1414; Found 382.1410.

Ethyl α-[[(cyclohexylidene)amino]oxy]benzeneacetate (3as)



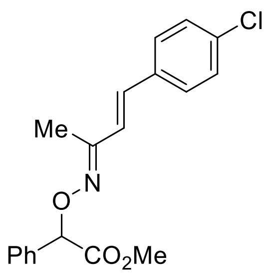
Oxime **2s** (29.4 mg, 0.26 mmol) was used. 31.2 mg, 45% yield. Purification by preparative TLC (hexane/AcOEt = 3/1→hexane/Et_2O = 2/1); A colorless oil; IR (neat) ν_{max} 1747 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.46 (m, 2H), 7.39-7.31 (m, 3H), 5.53 (s, 1H), 4.23-4.15 (m, 2H), 2.59 (t, J = 6.2 Hz, 2H), 2.21 (t, J = 6.4 Hz, 2H), 1.73-1.56 (m, 6H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.1, 162.6, 135.5, 128.6, 128.5, 127.5, 82.7, 61.0, 32.0, 27.0, 25.8, 25.79, 25.74, 14.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{21}O_3NNa$ 298.1414; Found 298.1410.

4-[(2-Ethoxy-2-oxo-1-phenylethoxy)imino]-1-piperidinecarboxylic acid 1,1-dimethylethyl ester (3at)



Oxime **2t** (55.7 mg, 0.26 mmol) was used. 58.2 mg, 62% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A colorless oil; IR (neat) ν_{max} 1749, 1687 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (br d, *J* = 7.3 Hz, 2H), 7.40-7.34 (m, 3H), 5.54 (s, 1H), 4.23-4.15 (m, 2H), 3.58-3.49 (m, 4H), 2.79-2.62 (m, 2H), 2.36-2.33 (m, 2H), 1.47 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.8, 158.6, 154.6, 135.0, 128.8, 128.6, 127.5, 82.9, 80.0, 77.3, 61.1, 30.9, 28.4, 26.0, 14.1; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{20}H_{28}O_5N_2Na$ 399.1890; Found 399.1890.

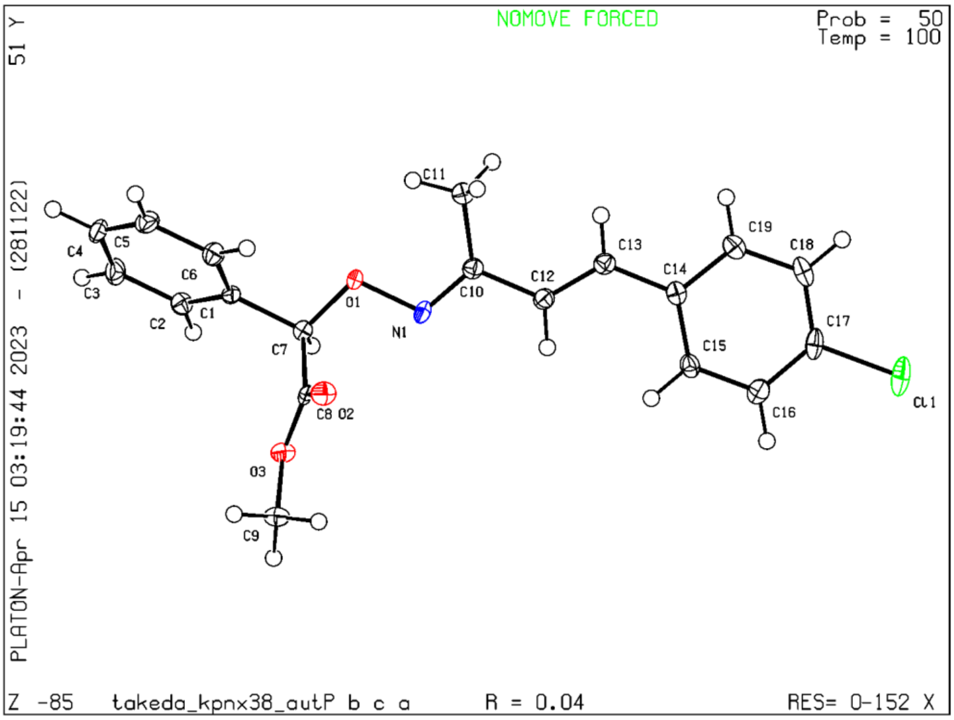
Methyl α-[[(*E*)-[(2*E*)-3-(4-Chlorophenyl)-1-methyl-2-propen-1-ylidene]amino]oxy]-benzeneacetate ((2*E*,3*E*)-8)



α-Keto ester **6** (35.4 μL, 0.25 mmol) and oxime (2*E*,3*E*)-**7** (50.9 mg, 0.26 mmol) were used. 76.2 mg, 89% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A white solid; Mp 115-116 °C; IR (KBr) ν_{max} 1754 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (m, 2H), 7.43-7.36 (m, 5H), 7.31 (br d, *J* = 7.2 Hz, 2H), 6.85 (d, *J* = 16.5 Hz, 1H), 6.78 (d, *J* = 16.5 Hz, 1H), 5.65 (s, 1H), 3.75 (s, 3H), 2.19 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.1, 157.5, 134.82, 134.76, 134.1, 132.5, 129.0, 128.9, 128.7, 128.0, 127.6, 126.2, 83.5, 52.3, 10.7; HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{19}H_{18}O_3N^{35}ClNa$ 366.0867; Found 366.0864.

The racemic crystal of (2*E*,3*E*)-**8** was obtained from (hexane/$CHCl_3$/Et_2O) solution. The single crystal of (2*E*,3*E*)-**8** ($C_{19}H_{18}O_3N^{35}Cl$) was used for the X-ray crystallographic analysis. A suitable crystal was measured on a dtrek-CrysAlisPro-abstract goniometer imported rigaku-d*trek images diffractometer. The crystal was kept at 100 K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimization.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (**2009**), *J. Appl. Cryst.* 42, 339-341.
2. Sheldrick, G.M. (**2015**). *Acta Cryst.* A71, 3-8.
3. Sheldrick, G.M. (**2015**). *Acta Cryst.* C71, 3-8.



X-ray structure of compound (2*E*,3*E*)-**8** (CCDC 2256541)

ORTEP of (2*E*,3*E*)-**8** with ellipsoid shown at the 50% contour percent probability level.

Bond precision: C-C = 0.0020 A Wavelength=0.71073

Cell:	a=11.0033(4)	b=15.9828(5)	c=19.3880(6)
	alpha=90	beta=90	gamma=90
Temperature:	100 K		

	Calculated	Reported
Volume	3409.64(19)	3409.64(19)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C19 H18 Cl N O3	C19 H18 Cl N O3
Sum formula	C19 H18 Cl N O3	C19 H18 Cl N O3
Mr	343.79	343.79
Dx,g cm-3	1.339	1.339
Z	8	8
Mu (mm-1)	0.240	0.240
F000	1440.0	1440.0
F000'	1441.81	
h,k,lmax	14,21,25	14,21,25
Nref	4123	4123
Tmin,Tmax	0.989,0.993	0.875,1.000
Tmin'	0.972	

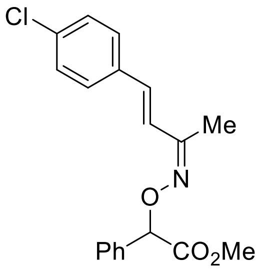
Correction method= # Reported T Limits: Tmin=0.875 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.000 Theta(max)= 28.000

R(reflections)= 0.0444(3294) wR2(reflections)= 0.0974(4123)

S = 1.025 Npar= 219

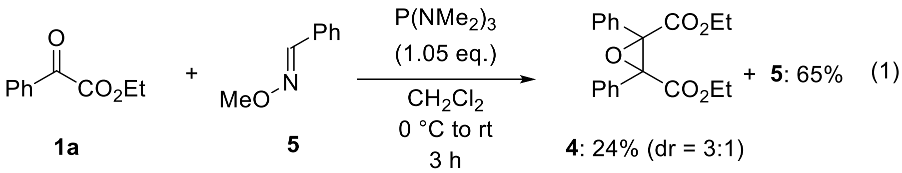
Methyl α-[[(*E*)-[(2*Z*)-3-(4-Chlorophenyl)-1-methyl-2-propen-1-ylidene]amino]oxy]-benzeneacetate ((2*Z*,3*E*)-8)



α-Keto ester **6** (35.4 μL, 0.25 mmol) and oxime (2 *Z*,3*E*)-**7** (50.9 mg, 0.26 mmol) were used. 58.0 mg, 67% yield. Purification by flash column chromatography (Biotage Isolera One, hexane/AcOEt = 5/1); A colorless oil; IR (neat) ν_{max} 1753 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57-7.48 (m, 3H), 7.46-7.36 (m, 5H), 7.32 (br d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 16.5 Hz, 1H), 5.63 (s, 1H), 3.75 (s, 3H), 2.11 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.3, 154.0, 135.5, 134.95, 134.85, 134.6, 129.0, 128.9, 128.70, 128.66, 127.7, 118.0, 83.4, 52.2, 16.9; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{19}H_{18}O_3N^{35}ClNa$ 366.0867; Found 366.0865.

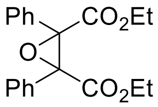
III. Additional experiments

(1) Scheme 1, Eq. 1



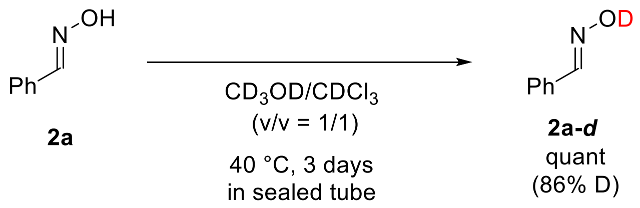
To a solution of α-keto ester **1a** (39.7 μL, 0.25 mmol) and *O*-methylated oxime **5** (35.1 mg, 0.26 mmol) in CH_2Cl_2 (2.5 mL) was slowly added $P(NMe_2)_3$ (47.3 μL, 0.26 mmol) at 0 °C under an argon atmosphere. After being stirred at the same temperature for 5 min, the reaction mixture was allowed to warm to room temperature for 3 h. The reaction mixture was diluted with $CHCl_3$ (5 mL), and concentrated under reduced pressure. The residue was purified by preparative TLC to afford epoxide **4** (20.1 mg, 24% yield, dr = 3:1) as a colorless oil and recovered *O*-methylated oxime **5** (22.7 mg, 65% recovered).

***rel*-2,3-Diethyl (2*R*,3*S*)-2,3-diphenyl-2,3-oxiranedicarboxylate (4)**



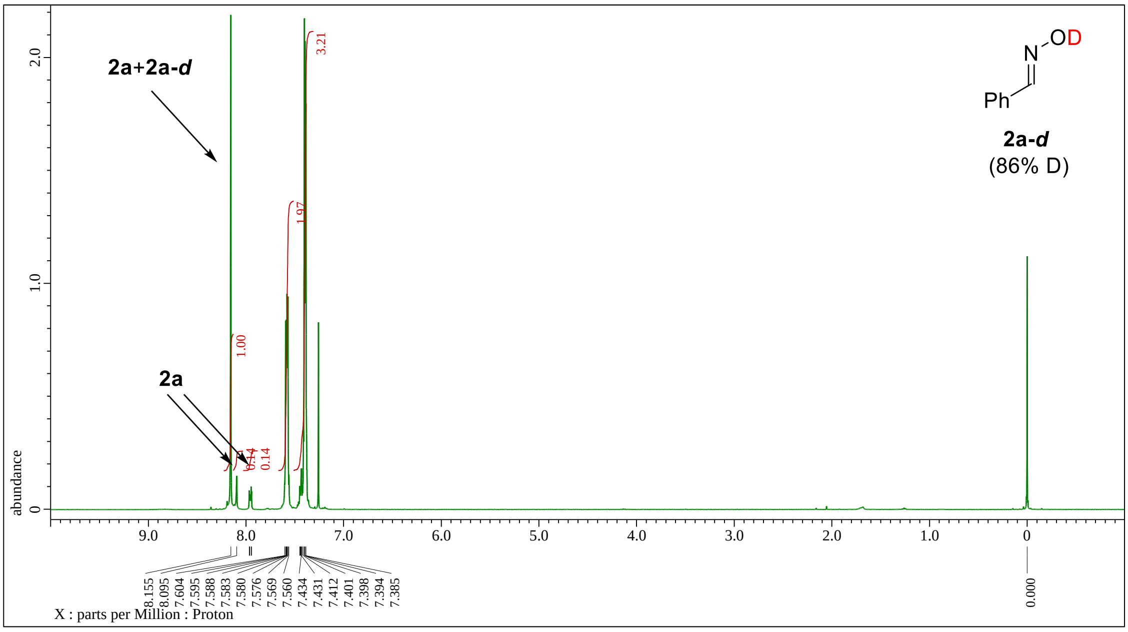
cis:*trans* or *trans*:*cis* = 3:1, The relative stereochemistry of the major diastereomer has not been established. A colorless oil; IR (neat) ν_{max} 1743 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (3:1 mixture of diastereomers) 7.76-7.74 (m, 1H), 7.40-7.32 (m, 5H), 7.16-7.12 (m, 4H), 4.27 (q, *J* = 7.2 Hz, 12/4H), 3.87 (q, *J* = 7.0 Hz, 4/4H), 1.30 (t, *J* = 7.1 Hz, 18/4H), 0.85 (t, *J* = 7.1 Hz, 6/4H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ (3:1 mixture of diastereomers) 166.9, 165.7, 131.4, 130.9, 129.0, 128.4, 128.0, 127.6, 127.5, 68.8, 68.5, 62.3, 61.6, 13.9, 13.5; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{20}H_{20}O_5Na$ 363.1203; Found 363.1202.

(2) Scheme 1, Eq. 2: Preparation of deuterium-labeled oxime 2a-*d*

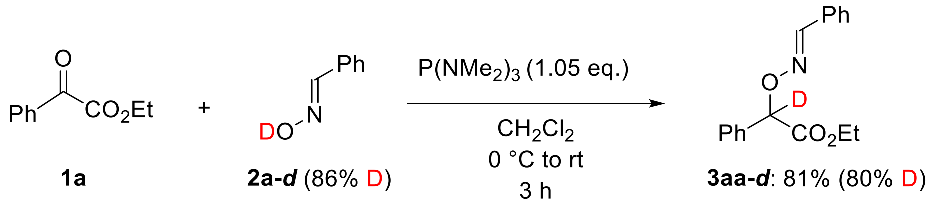


To a solution of *E*-benzaldehyde oxime (**2a**) (200.0 mg, 1.65 mmol) in $CDCl_3$ (1.5 mL) and CD_3OD (1.5 mL) in sealed tube was stirred at 40 °C under an argon atmosphere. After being stirred at the same temperature for 3 days, the reaction mixture was diluted with $CDCl_3$ (5 mL), and concentrated under reduced pressure. The crude product **2a-*d*** (200.9 mg, quant, 86% D) as a colorless oil was used without the further purification. By the comparison of chemical shifts and integration of ^{1}H NMR of hydrogen form and deuterated product, D contents of **2a-*d*** were determined.

^{1}H-NMR (400 MHz, $CDCl_3$)

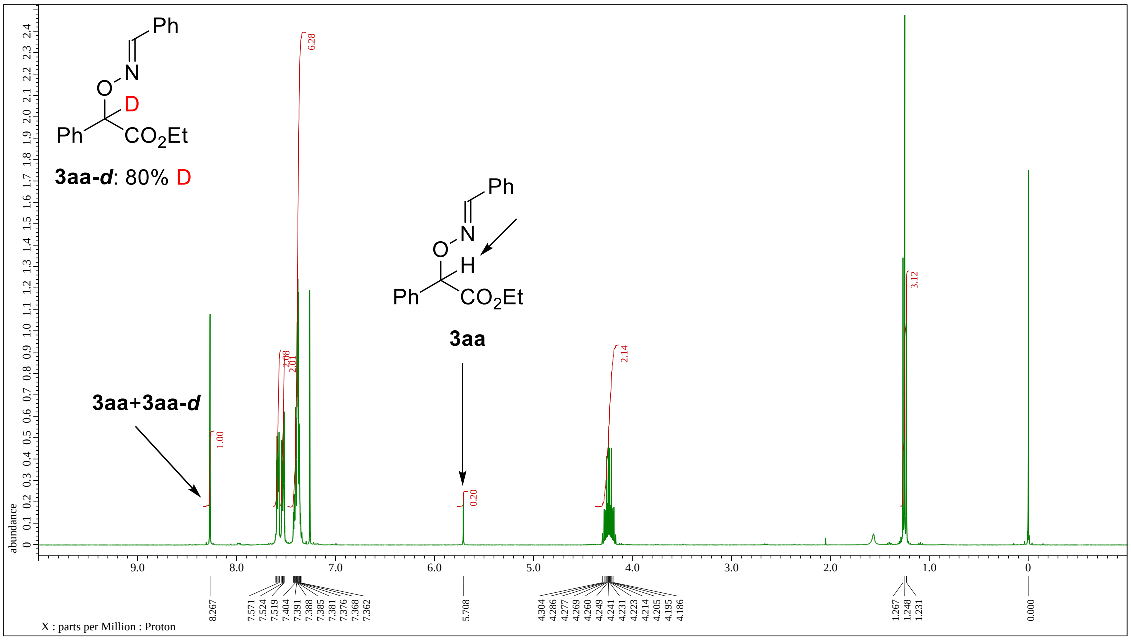


(3) Scheme 1, Eq. 2: a deuterium-labeled experiment

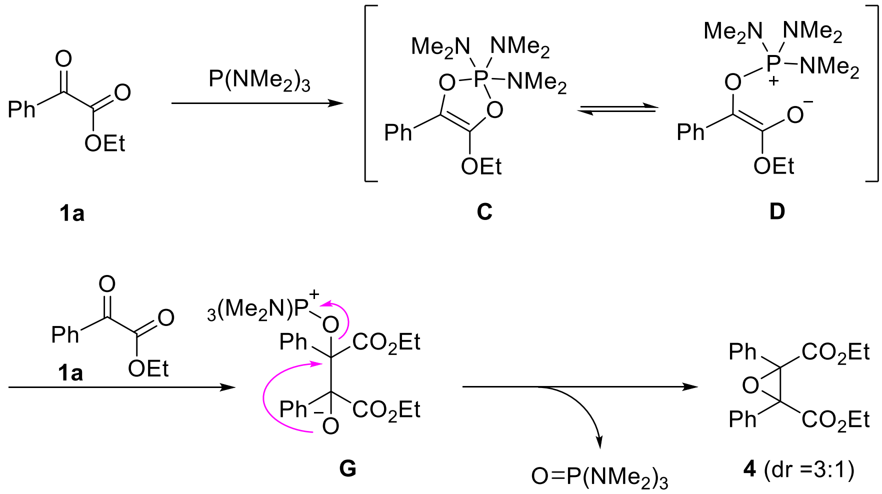


To a solution of α-keto ester **1a** (39.7 μL, 0.25 mmol) and oxime **2a-*d*** (31.8 mg, 0.26 mmol) in CH_2Cl_2 (2.5 mL) was slowly added $P(NMe_2)_3$ (47.3 μL, 0.26 mmol) at 0 °C under an argon atmosphere. After being stirred at the same temperature for 5 min, the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with $CHCl_3$ (5 mL), and concentrated under reduced pressure. The residue was purified by preparative TLC (hexane/AcOEt = 5/1) to afford oxime ether **3aa-*d*** (57.4 mg, 81% yield, 80% D) as a colorless oil. By the comparison of chemical shifts and integration of ^{1}H NMR of hydrogen form and deuterated product, D contents of **3aa-*d*** were determined.

^{1}H-NMR (400 MHz, $CDCl_3$)



(4) Proposed reaction pathway for the formation of epoxide



Based on the above results and the literature,[12,13] a plausible reaction pathway is proposed. Formal [4+1] cycloaddition of α-keto ester **1a** and $P(NMe_2)_3$ led to the formation of Kukhtin–Ramirez adducts **C** and **D** (KRAs). The nucleophilic addition of KRAs to the other **1a** generated alkoxyphosphonium intermediate **G**, which subsequently underwent cyclization to obtain epoxide **4**.

[12] Wilson, E. E.; Rodriguez, K. X.; Ashfeld, B. L., *Tetrahedron,* **2015**, *71*, 5765–5775.

[13] Ramirez, F.; Gulati, A. S.; Smith, C. P., *J. Org. Chem*., **1968**, *33*, 13–19.