Supporting Information
for

## Relative Reactivity of anti- and syn-Oximino-Carbonates and Carbamates of 2-Pyridyl Acetic Acid Esters

Ha Young Kim, Douglas A. Lantrip, and Philip L. Fuchs*
Department of Chemistry, Purdue University, West Lafayette, Indiana 47907

## Experimental

## General Procedure

All reagents purchased were used as received. Methylene chloride $\left(\mathrm{CH} \quad{ }_{2} \mathrm{Cl}_{2}\right)$ and dimethylsulfoxide (DMSO) were distilled from calcium hydride. Sodium sulfate was anhydrous.. All recrystallization, chromatographic, and work-up solvents were distilled. Glassware was oven dried and/or flamed dried. Reactions were carried out under a positive pressure of argon in anhydrous solvents, and the reaction flasks were fitted with rubber septa for the introduction of substrates and reagents via syringe. Progress of reactions was monitored by thin layer chromatography (TLC). TLC was performed on glass-backed silica gel 60 F 254 plates (EM reagents, 0.25 mm ) and eluted with ( $\mathrm{v} / \mathrm{v}$ ) EtOAc in hexane. TLC plates were visualized with UV ( 254 nm ) and/or with TLC staining solution activated with heat. The commonly employed TLC visualizing solution was p -anisaldehyde solution ( 360 mL absolute ethanol, 20 mL concentrated $\mathrm{H}_{2} \mathrm{SO}_{4}, 4 \mathrm{~mL}$ glacial acetic acid, $20 \mathrm{~mL} p$-anisaldehyde).

Analytical samples were obtained from flash silica gel chromatography ( sgc ), using silica gel of 230400 mesh, or from recrystallization of the crude products. Melting points were obtained on a MEL-TEMP capillary melting point apparatus and are uncorrected. ${ }^{1} \mathrm{H}-\mathrm{NMR}$ and ${ }^{13} \mathrm{NMR}$ spectra were recorded on a Varian $300(300 \mathrm{MHz})$ spectrometer. NMR spectra were determined in chloroform-d ${ }_{1}\left(\mathrm{CDCl}_{3}\right)$ or dimethylsulfoxide- $\mathrm{d}_{6}$ (DMSO- $\mathrm{d}_{6}$ ) solution and reported in parts million (ppm) from the residual chloroform ( 7.27 ppm and 77.23 ppm ) or DMSO ( 2.50 ppm and 39.51 ppm ) standard, respectively. Peak multiplicities in ${ }^{1} \mathrm{H}$-NMR spectra, when reported, are abbreviated as s (singlet), d (doublet), t (triplet), m multiplet, and/or br (broad). Mass spectra were run by the Purdue University campus wide mass spectrometry facility. The low resolution El and Cl (isobutane) spectra were obtained in a Finnigan 4000 mass spectrometer with a Nova 4 data system with the molecular ion designated as " $\mathrm{M}^{+\prime}$. The high resolution mass spectra were obtained on a Kratos MS-50 instrument. Compounds characterized by exact mass were homogeneous by TLC and NMR. NMR shift assignment were performed by analogy to known compounds and should be regarded as tentative.

## General procedure for the preparation of 2- or 4-Pyridylacetate 6, 23, 24.

To a suspended solution of 2- or 4-pyridylacetic acid hydrochloride ( 3.0 mmol ) and alcohol (allyl or tbutyl alcohol, 4.5 mmol ) in 15 mL of dichloromethane was added triethylamine ( 6.0 mmol ), $1,3-$ dicyclohexylcarbodiimide ( 3.0 mmol ) and a catalytic amount of 4 -(dimethylamino) pyridine ( 0.15 mmol ) at $25^{\circ} \mathrm{C}$. After stirring 12 h at $45^{\circ} \mathrm{C}$, the reaction mixture was filtered through a Büchner funnel to remove 1,3dicyclohexylurea. The filterate was washed with water ( $15 \mathrm{~mL} \times 3$ ) and dried over anhydrous sodium sulfate. Purification by column chromatography ( $25 \%$ EtOAc/hexane) afforded the desired ester of 2 - or 4pyridylacetic acid 6, 23, 24.

Allyl 2-pyridylacetate 6, yield: $81 \%$, yellow liquid; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.37 ;{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.59(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}), 7.69(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.6,7.6 \mathrm{~Hz}), 7.29(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.6 \mathrm{~Hz}), 7.32(1 \mathrm{H}, \mathrm{m}), 5.89(1 \mathrm{H}, \mathrm{m})$, $5.30(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.2 \mathrm{~Hz}), 5.24(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.4 \mathrm{~Hz}), 4.66(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.6 \mathrm{~Hz}), 3.91(2 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( 75 MHz , $\mathrm{CDCl}_{3}$ ) $\delta 170.34,154.53,149.63,136.74,132.14,124.00,122.25,118.36,65.64,43.99 ; \mathrm{MS}(\mathrm{El}) \mathrm{m} / \mathrm{z}$ (relative intensity): $178\left(\mathrm{M}^{+}+\mathrm{H}\right), 162\left(\mathrm{M}-\mathrm{CH}_{3}\right), 134\left(\mathrm{M}-\mathrm{C}_{3} \mathrm{H}_{7}, 32\right), 92\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{5} \mathrm{O}_{2}, 100\right) ; \mathrm{MS}(\mathrm{Cl}) \mathrm{m} / \mathrm{z}: 178$ ( $\mathrm{M}+\mathrm{H}$, base peak).
t-Butyl 2-pyridylacetate 23, yield: 74\%, light yellow oil; TLC (EA:hex = 2:1), $\mathrm{R}_{\mathrm{f}} 0.60$; ${ }^{1} \mathrm{H}$ NMR ( 300 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 8.53(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}), 7.62(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.7,7.7 \mathrm{~Hz}), 7.27(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.7 \mathrm{~Hz}), 7.14(1 \mathrm{H}, \mathrm{m}), 3.75$ $(2 \mathrm{H}, \mathrm{s}), 1.44(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 169.82,155.05,149.33,136.41,123.80,121.86,80.87$, 45.10, 28.03; MS (EI) m/z (relative intensity): 193 ( $\mathrm{M}^{+}$), $120\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{9} \mathrm{O}_{1}, 9\right), 92\left(\mathrm{M}-\mathrm{C}_{5} \mathrm{H}_{9} \mathrm{O}_{2}, 18\right), 57\left(\mathrm{C}_{4} \mathrm{H}_{9}\right.$, 100); MS (Cl) m/z: 194 (M+H, base peak).

Allyl 4-pyridylacetate 24, yield: 75\%, light yellow liquid; TLC (EA:hex $=2: 1$ ), $\mathrm{R}_{\mathrm{f}} 0.47 ;{ }^{1} \mathrm{H} \mathrm{NMR}(300 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta 8.45(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.0 \mathrm{~Hz}), 7.12(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.0 \mathrm{~Hz}), 5.78(1 \mathrm{H}, \mathrm{m}), 5.17(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=18.8 \mathrm{~Hz}), 5.13(1 \mathrm{H}$, $\mathrm{d}, \mathrm{J}=10.3 \mathrm{~Hz}), 4.51(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.6 \mathrm{~Hz}), 3.55(2 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 169.79,150.12,142.85$, $131.88,124.68,118.74,65.90,40.62 ; \mathrm{MS}(\mathrm{El}) \mathrm{m} / \mathrm{z}$ (relative intensity): $177\left(\mathrm{M}^{+}, 8\right), 120\left(\mathrm{M}-\mathrm{C}_{3} \mathrm{H}_{5} \mathrm{O}_{1}, 35\right), 92$ $\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{5} \mathrm{O}_{2}, 100\right)$; $\mathrm{MS}(\mathrm{Cl}) \mathrm{m} / \mathrm{z}$ : $178(\mathrm{M}+\mathrm{H}$, base peak).

## General procedure ${ }^{1}$ for the preparation of anti- or syn-Oxime ester 7a, 7s, 12a, 12s, 25a/25s.

To a solution of 2- or 4-pyridylacetate (allyl ester or t-butyl ester 6, 23, 24, 4.0 mmol ) and excess acetic acid ( 1.5 mL ) was added dropwise a solution of sodium nitrite ( 4.0 mmol ) in water ( 3.0 mL ) at $0^{\circ} \mathrm{C}$. An additional 3.0 mL of water was added to facilitate stirring and the reaction mixture was allowed to slowly warm to room temperature over 3 h . The aqueous solution was extracted with dichloromethane ( 10 mL x 2) and the organic layer was washed twice with water ( $10 \mathrm{~mL} \times 2$ ). The dichloromethane layer was dried over anhydrous sodium sulfate and concentrated by evaporation. Anti- and syn-oximes were separated by flash column chromatography ( $20 \%$ EtOAc/hexane) affording $7 \mathrm{a} / 7 \mathrm{~s}$ (1/3 ratio, quantitative yield), 12a/12s (1.0/1.4 ratio, quantitative yield), 25a/25s ( $93 \%$ yield).

Allyl $\alpha$-anti-oximino- $\alpha$-(2-pyridyl)acetate 7a, light yellow solid; mp $95-96^{\circ} \mathrm{C}$; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.29$; ${ }^{1} \mathrm{H}$ NMR $\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.58(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.0 \mathrm{~Hz}), 8.17(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=8.1 \mathrm{~Hz}), 8.01(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.8,8.1 \mathrm{~Hz})$, $7.55(1 \mathrm{H}, \mathrm{m}), 6.15-6.01(1 \mathrm{H}, \mathrm{m}), 5.48(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=16.9 \mathrm{~Hz}), 5.35(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.3 \mathrm{~Hz}), 4.90(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.8 \mathrm{~Hz})$; ${ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 163.63$, 149.93, 145.53, 143.10, 138.84, 131.68, 125.83, 124.06, 119.57, 66.78; MS (Cl) m/z: 207 ( $\mathrm{M}+\mathrm{H}$, base peak).

Allyl $\alpha$-syn-oximino- $\alpha$-(2-pyridyl)acetate 7s, light yellow solid; mp $84.5-86^{\circ} \mathrm{C}$; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.39$; ${ }^{1} \mathrm{H}$ NMR $\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 9.88(1 \mathrm{H}, \mathrm{brs}) 8.66(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}), 7.88(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=8.1 \mathrm{~Hz}), 7.77(1 \mathrm{H}$, dd, $J=7.7,8.1 \mathrm{~Hz}), 7.36(1 \mathrm{H}, \mathrm{m}), 6.11-5.98(1 \mathrm{H}, \mathrm{m}), 5.50(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.1 \mathrm{~Hz}), 5.32(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.3 \mathrm{~Hz}), 4.96$ (2H, d, J=5.9 Hz); ${ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 163.35,151.71,150.50,149.61,137.21,131.66,124.75$, 121.19, 119.31, 66.71; MS (EI) m/z (relative intensity): $207\left(\mathrm{M}^{+}+\mathrm{H}, 7\right), 176(\mathrm{M}-\mathrm{NO}), 121\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{5} \mathrm{O}_{2}, 62\right)$, $105\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{5} \mathrm{O}_{3}, 100\right), 78\left(\mathrm{C}_{5} \mathrm{H}_{4} \mathrm{~N}_{1}, 86\right)$; MS (Cl) m/z: $207(\mathrm{M}+\mathrm{H}$, base peak).
t-Butyl $\alpha$-anti-oximino- $\alpha$-(2-pyridyl)acetate 12a, white solid; mp $131-132.5^{\circ} \mathrm{C}$; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.31$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.57(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}), 7.97(2 \mathrm{H}, \mathrm{m}), 7.51(1 \mathrm{H}, \mathrm{m}), 1.63(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 162.90,149.73,145.72,144.85,138.26,125.30,123.85,83.22,28.05 ; \mathrm{MS}(\mathrm{Cl}) \mathrm{m} / \mathrm{z}:$ 223 (M+H, base peak).
t-Butyl $\alpha$-syn-oximino- $\alpha$-(2-pyridyl)acetate 12s, white solid; mp $133.5-134^{\circ} \mathrm{C}$; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.43$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 9.45(1 \mathrm{H}, \mathrm{brs}), 8.66(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}), 7.77(2 \mathrm{H}, \mathrm{m}), 7.32(1 \mathrm{H}, \mathrm{m}), 1.65(9 \mathrm{H}$, $\mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 162.84,151.69,150.67,149.45,136.76,124.16,121.06,84.12,28.28 ;$ MS (EI) m/z (relative intensity): $207\left(\mathrm{M}-\mathrm{CH}_{3}\right), 166\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{8}, 59\right), 105\left(\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{~N}_{21}, 100\right), 78\left(\mathrm{C}_{5} \mathrm{H}_{4} \mathrm{~N}_{1}, 20\right), 57$ $\left(\mathrm{C}_{4} \mathrm{H}_{9}, 78\right)$; MS (CI) m/z: 223 (M+H, base peak).

Allyl $\alpha$-oximino- $\alpha$-(4-pyridyl)acetate 25a/25s mixture, pale yellow solid; TLC (EA:hex = 2:1), $R_{f} 0.49$ (anti), $\mathrm{R}_{\mathrm{f}} 0.57$ (syn); ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{DMSO}_{6}$ ) $\delta 12.92$ (anti, 1H, brs), 12.67 (syn, 1H, brs), 8.67 (anti, $2 \mathrm{H}+\operatorname{syn} 2 \mathrm{H}, \mathrm{m}$ ), 7.48 (syn, 2H, d, J=4.6 Hz), 7.42 (anti, $2 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.5 \mathrm{~Hz}$ ), 6.05-5.92 (anti, $1 \mathrm{H}+\operatorname{syn}, 1 \mathrm{H}$, m), 5.48-5.24 (anti, $2 \mathrm{H}+\operatorname{syn}, 2 \mathrm{H}, \mathrm{m}$ ), 4.89 (syn, $2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.6 \mathrm{~Hz}$ ), 4.75 (syn, $2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.5 \mathrm{~Hz}$ ); MS (EI) m/z: $206\left(\mathrm{M}^{+}\right)$; MS (CI) m/z: $207(\mathrm{M}+\mathrm{H}$, base peak).

General procedure ${ }^{2}$ for the preparation of Methyl anti- or syn-carbonate 8a, 8s, 13a, 13s.

To a solution of pure $\alpha$-anti- or $\alpha$-syn-oximino- $\alpha$-(2-pyridyl)acetate (7a, 7s, 12a, 12s, 1.0 mmol ) in 5.0 mL of dichloromethane was added triethylamine ( 2.0 mmol ) and methyl chloroformate ( 1.05 mmol ) at $25^{\circ} \mathrm{C}$. After stirring 30 min , the resulting solution was added 5.0 mL of water and extracted with dichloromethane ( $5.0 \mathrm{~mL} \times 3$ ). The organic layer was dried over anhydrous sodium sulfate and concentrated to give methyl anti- or syn-oximino carbonate 8a, 8s, 13a, 13s.

Allyl $\alpha$-anti-(methoxycarbonyl)oximino- $\alpha$-(2-pyridyl)acetate 8a, yield: 99\%, colorless oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.31 ;{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.75(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.6 \mathrm{~Hz}), 7.87(2 \mathrm{H}, \mathrm{m}), 7.44(1 \mathrm{H}, \mathrm{m}), 6.09-5.96$ $(1 \mathrm{H}, \mathrm{m}), 5.45(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.2 \mathrm{~Hz}), 5.33(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.2 \mathrm{~Hz}), 4.89(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.7 \mathrm{~Hz}) 3.97(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR $\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 162.34,155.31,153.47,150.04,147.25,136.85,131.24,126.74,125.59,119.80$, 67.57, 56.23; MS (CI) m/z: 265 (M+H, base peak).

Allyl $\alpha$-syn-(methoxycarbonyl)oximino- $\alpha$-(2-pyridyl)acetate 8s, yield: quantitative, colorless oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.48$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.67(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.7 \mathrm{~Hz}), 8.14(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.9 \mathrm{~Hz}), 7.81$ ( $1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=6.0,7.9 \mathrm{~Hz}$ ), $7.42(1 \mathrm{H}, \mathrm{m}), 6.10-6.00(1 \mathrm{H}, \mathrm{m}), 5.50(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.2 \mathrm{~Hz}), 5.34(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.4 \mathrm{~Hz})$, $4.97(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.3 \mathrm{~Hz}) 3.96(3 \mathrm{H}, \mathrm{s}) ;{ }^{3}{ }^{3} \mathrm{H} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 161.08,157.13,153.32,149.81,148.53$, 136.95, 131.03, 125.96, 122.17, 119.28, 66.81, 55.81; MS (EI) m/z (relative intensity): 264 ( $\mathrm{M}^{+}, 1$ ), 220 $\left(\mathrm{M}-\mathrm{CO}_{2}, 3\right), 105\left(\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{~N}_{2}, 42\right), 78\left(\mathrm{C}_{5} \mathrm{H}_{4} \mathrm{~N}_{1}, 100\right)$; MS (Cl) m/z: $265(\mathrm{M}+\mathrm{H}$, base peak).
t-Butyl $\alpha$-anti-(methoxycarbonyl)oximino- $\alpha$-(2-pyridyl)acetate 13a, yield: 93\%, light green oil; TLC (EA:hex $=1: 2), \mathrm{R}_{\mathrm{f}} 0.37$; ${ }^{1} \mathrm{H}$ NMR $\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.72(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.7 \mathrm{~Hz}), 7.82(2 \mathrm{H}, \mathrm{m}), 7.40(1 \mathrm{H}, \mathrm{m}), 3.93(3 \mathrm{H}$, $\mathrm{s}), 1.59(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 161.19,156.10,153.38,149.64,147.56,136.44,126.25$, 125.02, 84.52, 55.74, 27.95; MS (CI) m/z: 281 (M+H, base peak).
t-Butyl $\alpha$-syn-(methoxycarbonyl)oximino- $\alpha$-(2-pyridyl)acetate 13s, yield: quantitative, light green oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.51$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.69(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.6 \mathrm{~Hz}), 8.12(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.9 \mathrm{~Hz}), 7.79$ $(1 \mathrm{H}, \mathrm{m}), 7.40(1 \mathrm{H}, \mathrm{m}), 3.97(3 \mathrm{H}, \mathrm{s}), 1.66(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 160.40,157.62,153.53$, 149.81, 148.83, 136.72, 125.64, 122.19, 85.12, 55.60, 28.21; MS (EI) m/z (relative intensity): 265 (M$\left.\mathrm{CH}_{8}\right), 224\left(\mathrm{M}-\mathrm{C}_{4} \mathrm{H}_{8}, 27\right), 57\left(\mathrm{C}_{4} \mathrm{H}_{9}, 100\right)$; MS (Cl) m/z: 281 (M+H, base peak).

## General procedure for the preparation of trans-2-Methylcyclohexyl anti- or syn-carbonate 9a, 9s, 14a,

 14s, 10a/10s.A solution of trans-2-methylcyclohexanol ( 1.00 mmol ), pyridine ( 1.33 mmol ) and triphosgene ( 0.33 mmol ) in 4.0 mL of dichloromethane was heated on an oil bath for 1.5 h at $50^{\circ} \mathrm{C}$ and cooled to $25^{\circ} \mathrm{C}$. To this solution was added a solution of anti- or syn-oxime (7a, 7s, 12a, 12s, 25a/25s, 1.00 mmol ) and trethylamine $(2.00 \mathrm{mmol})$ in 3.0 mL of dichloromethane through cannula. This reaction mixture was stirred for 1.5 h at $25^{\circ} \mathrm{C}$, quenched with 5.0 mL of water and extracted with dichloromethane ( $5.0 \mathrm{~mL} \times 3$ ). The combined organic layer was washed with water ( $5.0 \mathrm{~mL} \times 2$ ), dried over anhydrous sodium sulfate and concentrated to yield trans-2-methylcyclohexyl anti- or syn-carbonate 9a, 9s, 14a, 14s, 10a/10s.

Allyl $\alpha$-anti-[(trans-2-methylcyclohexyloxy)carbonyl]oximino- $\alpha-(2$-pyridyl)acetate 9a, yield: 97\%, light purple oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.50$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.75(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.7 \mathrm{~Hz}), 7.90(2 \mathrm{H}, \mathrm{m})$, $7.43(1 \mathrm{H}, \mathrm{m}), 6.09-5.99(1 \mathrm{H}, \mathrm{m}), 5.45(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.3 \mathrm{~Hz}), 5.32(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.4 \mathrm{~Hz}), 4.89(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.8 \mathrm{~Hz})$, $4.45(1 \mathrm{H}, \mathrm{m}), 2.14(1 \mathrm{H}, \mathrm{m}), 1.84-1.04(8 \mathrm{H}, \mathrm{m}), 0.98(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.4 \mathrm{~Hz})$; ${ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ 162.23, 154.67, 152.52, 149.67, 147.12, 136.61, 131.06, 126.53, 125.25, 119.30, 84.81, 67.11, 37.16, 33.37, 31.40, 25.06, 24.60, 18.28; MS (EI) m/z: 347 (M+H); MS (CI) m/z: 347 (M+H, base peak).

Allyl $\alpha$-syn-[(trans-2-methylcyclohexyloxy)carbonyl]oximino- $\alpha$-(2-pyridyl)acetate 9s, yield: quantitative, light purple oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.53 ;{ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.67(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.9 \mathrm{~Hz}$ ), 8.15 $(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.9 \mathrm{~Hz}), 7.80(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.8,7.9 \mathrm{~Hz}), 7.41(1 \mathrm{H}, \mathrm{m}), 6.10-5.97(1 \mathrm{H}, \mathrm{m}), 5.50(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=17.2 \mathrm{~Hz})$,
$5.32(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=10.5 \mathrm{~Hz}), 4.98(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.2 \mathrm{~Hz}), 4.43(1 \mathrm{H}, \mathrm{m}), 2.16(1 \mathrm{H}, \mathrm{m}), 2.06-1.10(8 \mathrm{H}, \mathrm{m}), 1.00(3 \mathrm{H}$, $\mathrm{d}, \mathrm{J}=6.7 \mathrm{~Hz}$ ); ${ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 161.25,156.77$, 152.64, 149.75, 149.18, 136.89, 131.13, 125.81, 122.14, 119.04, 84.64, 66.66, 37.24, 33.40, 31.43, 25.11, 24.64, 18.32; MS (EI) m/z: $347\left(\mathrm{M}^{+}+\mathrm{H}\right)$; MS (CI) m/z: 347 ( $\mathrm{M}+\mathrm{H}$, base peak).
t-Butyl $\alpha$-anti-[(trans-2-methylcyclohexyloxy)carbonyl]oximino- $\alpha$-(2-pyridyl)acetate 14a, yield: 98\%, light purple oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.57 ;{ }^{1} \mathrm{H} \mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.72(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.7 \mathrm{~Hz}), 7.83(2 \mathrm{H}, \mathrm{m})$, $7.39(1 \mathrm{H}, \mathrm{m}), 4.41(1 \mathrm{H}, \mathrm{m}), 2.15(1 \mathrm{H}, \mathrm{m}), 1.80-0.96(8 \mathrm{H}, \mathrm{m}), 1.59(9 \mathrm{H}, \mathrm{s}), 0.98(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.4 \mathrm{~Hz}) ;{ }^{13} \mathrm{H}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 163.37,155.70,152.69,149.57,147.66,136.45,126.33,124.94,84.52,84.28$, 37.14, 33.36, 31.40, 27.94, 25.06, 24.59, 18.28; MS (ESI, positive): $363[\mathrm{M}+\mathrm{H}]^{+}, 385\left([\mathrm{M}+\mathrm{Na}]^{+}\right.$, base peak); HRMS (ESI, positive): calcd. for $\mathrm{C}_{19} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{5} 363.1920$, found 363.1917.
t-Butyl $\alpha$-syn-[(trans-2-methylcyclohexyloxy)carbonyl]oximino- $\alpha$-(2-pyridyl)acetate 14s, yield: 98\%, light purple oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.63$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.69(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.8 \mathrm{~Hz}), 8.13(1 \mathrm{H}, \mathrm{d}$, $J=8.0 \mathrm{~Hz}), 7.79(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.7,8.0 \mathrm{~Hz}), 7.40(1 \mathrm{H}, \mathrm{m}), 4.43(1 \mathrm{H}, \mathrm{m}), 2.17(1 \mathrm{H}, \mathrm{m}), 1.85-0.97(8 \mathrm{H}, \mathrm{m}), 1.67$ ( $9 \mathrm{H}, \mathrm{s}$ ), $1.03(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.5 \mathrm{~Hz}) ;{ }^{13} \mathrm{H} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 160.59,157.50,152.78,149.77,148.99$, 136.66, 125.54, 122.11, 84.89, 84.22, 37.21, 33.34, 31.39, 28.21, 25.06, 24.59, 18.26; MS (ESI, positive): $363[\mathrm{M}+\mathrm{H}]^{+}, 385\left([\mathrm{M}+\mathrm{Na}]^{+}\right.$, base peak); HRMS (ESI, positive): calcd. for $\mathrm{C}_{19} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{5} 363.1920$, found 363.1913.

Allyl $\alpha-[($ trans-2-methylcyclohexyloxy)carbonyl]oximino- $\alpha$-(4-pyridyl)acetate 10a/10s mixture, yield: 91\%, pale yellow oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.40(\mathrm{a} / \mathrm{s}) ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.79-8.74$ (anti, $2 \mathrm{H}+$ syn, $2 \mathrm{H}, \mathrm{m}), 7.60(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.2 \mathrm{~Hz}), 7.38(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.1 \mathrm{~Hz}), 6.08-5.94$ (anti, $1 \mathrm{H}+\operatorname{syn}, 1 \mathrm{H}, \mathrm{m}), 5.52-5.32$ (anti, $2 \mathrm{H},+\operatorname{syn}, 2 \mathrm{H}, \mathrm{m}), 4.95(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.8 \mathrm{~Hz}), 4,85(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.8 \mathrm{~Hz}), 4.48-4.37$ (anti, 1H + syn, 1H, m), 2.170.93 (anti, $9 \mathrm{H}+$ syn, $9 \mathrm{H}, \mathrm{m}$ ), $1.00(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.4 \mathrm{~Hz}), 0.94(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.4 \mathrm{~Hz}) ; \mathrm{MS}(\mathrm{El}) \mathrm{m} / \mathrm{z}: 347\left(\mathrm{M}^{+}+\mathrm{H}\right) ; \mathrm{MS}$ (Cl) m/z: $347(\mathrm{M}+\mathrm{H}$, base peak).

## General procedure ${ }^{3}$ for the preparation of (S)- $\alpha$-Methylbenzyl anti- or syn-carbamate $\mathbf{1 5 a}, \mathbf{1 5 s}$.

A mixture solution of anti- or syn-oxime (7a or 7s, 1.00 mmol ), (S)-(-)- $\alpha$-methylbenzyl isocyanate (1.10 mmol ) and triethylamine ( 2.05 mmol ) in 5.0 mL of dichloromethane was heated on an oil bath for 10 h at $50^{\circ} \mathrm{C}$. The resulting solution was combined with 10 mL of water and extracted dichloromethane ( 15 mL x 2). The organic layer was dried over anhydrous sodium sulfate and concentrated through a rotary evaporator. Purification by flash column chromatography ( $25 \%$ EtOAc/hexane) provided carbamate 15a, 15s.
t-Butyl $\alpha$-anti-\{[(S)- $\alpha$-methylbenzyl]carbamoyl\}oximino- $\alpha$-(2-pyridyl)acetate 15a, yield: quantitative, white solid; mp 152-154${ }^{\circ} \mathrm{C}$; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.31 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.73(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.2 \mathrm{~Hz})$, $7.97(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=8.1 \mathrm{~Hz}), 7.86(1 \mathrm{H}$, dd, J=7.8, 7.9 Hz$), 7.41-7.30(6 \mathrm{H}, \mathrm{m}), 6.72(1 \mathrm{H}$, br-d, J=7.2 Hz), 5.04 $(1 \mathrm{H}, \mathrm{m}), 1.65(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.7 \mathrm{~Hz}), 1.59(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{H} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 161.43,153.29,149.69$, $147.53,145.76,136.85,129.00,127.86,127.02,126.33,125.30,124.08,84.59,51.36,28.20,22.31$; MS (EI) m/z: $369\left(\mathrm{M}^{+}\right)$; MS (CI) m/z: $370(\mathrm{M}+\mathrm{H})$; MS (ESI, positive): 392 ([M+Na] ${ }^{+}$, base peak).
t-Butyl $\alpha$-syn-\{[(S)- $\alpha$-methylbenzyl]carbamoyl\}oximino- $\alpha$-(2-pyridyl)acetate 15s, yield: 99\%, light yellow oil; TLC (EA:hex = 1:2), $\mathrm{R}_{\mathrm{f}} 0.43$; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.70(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.7 \mathrm{~Hz}), 7.97(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.7$ $\mathrm{Hz}), 7.81(1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=7.7,7.9 \mathrm{~Hz}), 7.44-7.30(6 \mathrm{H}, \mathrm{m}), 6.19(1 \mathrm{H}, \mathrm{br}-\mathrm{d}, \mathrm{J}=6.7 \mathrm{~Hz}), 5.06(1 \mathrm{H}, \mathrm{m}), 1.67(9 \mathrm{H}, \mathrm{s})$, $1.64(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{H} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 161.25,153.11,149.93,147.23,145.55$, 142.87, 137.27, 129.00, 127.85, 126.41, 125.82, 122.16, 85.47, 51.32, 28.49, 22.18; MS (El) m/z (relative intensity): $369\left(\mathrm{M}^{+}\right)$, $105\left(\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{~N}_{2}, 51\right), 57\left(\mathrm{C}_{4} \mathrm{H}_{9}, 100\right)$; MS (CI) m/z: $370(\mathrm{M}+\mathrm{H})$; MS (ESI, positive): 370 $[\mathrm{M}+\mathrm{H}]^{+}, 392\left([\mathrm{M}+\mathrm{Na}]^{+}\right.$, base peak).
$\alpha$-Oximino- $\alpha-(2$-pyridyl)acetic acid 19a/19s.
A solution of t-butyl $\alpha$-oximino- $\alpha$-(2-pyridyl)acetate 12a/12s ( $0.10 \mathrm{~g}, 0.45 \mathrm{mmol}$ ) and trifluoroacetic acid $\left(0.35 \mathrm{~mL}, 4.50 \mathrm{mmol}\right.$ ) in 5.0 mL of dichloromethane was stirred 16 h at $25^{\circ} \mathrm{C}$. The resulting solution was concentrated to one-third volume and treated with hexane. The triturated solid was collected by decantation, washing with hexane, to give the desired oximino-acids 19a/19s, yield: quantitative, light yellow solid; TLC (EA:hex = 2:1), origin spot; ${ }^{1} \mathrm{H}$ NMR ( $\left.300 \mathrm{MHz}, \mathrm{DMSO}^{2} \mathrm{~d}_{6}\right) \delta 8.69(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.1 \mathrm{~Hz}$ ), 8.59 (1H, d, J=4.4 Hz), 8.01-7.73 (anti, $2 \mathrm{H}+$ syn, $2 \mathrm{H}, \mathrm{m}$ ), 7.53-7.43 (anti, $1 \mathrm{H}+$ syn, $1 \mathrm{H}, \mathrm{m}$ ); MS (ESI, positive): $167[\mathrm{M}+\mathrm{H}]^{+}$; HRMS (ESI, positive): calcd. for $\mathrm{C}_{7} \mathrm{H}_{6} \mathrm{~N}_{2} \mathrm{O}_{3} 167.0457$, found 167.0455.

## General procedure for the preparation of acid-catalyzed deprotected acid 16s, 17s, 18s.

A solution of the t-butyl ester of $\alpha$-syn-oxime derivative (13s, 14s, 15s, 0.2 mmol ) and trifluoroacetic acid ( 2.0 mmol ) in 2.0 mL of dichloromethane was stirred for $6 \sim 48 \mathrm{~h}$ at $25^{\circ} \mathrm{C}$. The resulting solution was concentrated to half volume and triturated with diethyl ether/hexane to give 16s, 17s, and with $\mathrm{MeOH} /$ ether/hexane to give 18s.
$\alpha$-syn-(Methoxycarbonyl)oximino- $\alpha$-(2-pyridyl)acetic acid 16s, yield: $99 \%$, white solid; mp $42^{\circ} \mathrm{C}$ (softens), $88-90^{\circ} \mathrm{C}$ (dec.); TLC (EA:hex = 1:2), origin spot; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{DMSO}-\mathrm{d}_{6}$ ) $\delta 8.73(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.6 \mathrm{~Hz}$ ), 8.03-8.01 (2H, m), 7.65 ( $1 \mathrm{H}, \mathrm{dd}, \mathrm{J}=4.4,4.8 \mathrm{~Hz}$ ), 3.91 (3H, s); MS (ESI, positive): $225[\mathrm{M}+\mathrm{H}]^{+}$.
$\alpha$-syn-[(trans-2-Methylcyclohexyloxy)carbonyl]oximino- $\alpha$-(2-pyridyl)acetic acid 17s, yield: $88 \%$, white solid; mp $87^{\circ} \mathrm{C}$ (dec.); TLC (EA:hex = 1:2), origin spot; ${ }^{1} \mathrm{H}$ NMR ( 300 MHz , DMSO-d ) $\delta 8.71$ ( $1 \mathrm{H}, \mathrm{d}, \mathrm{J}=3.5$ $\mathrm{Hz}), 8.00(2 \mathrm{H}, \mathrm{m}), 7.61(1 \mathrm{H}, \mathrm{m}), 4.36(1 \mathrm{H}, \mathrm{m}), 2.02(1 \mathrm{H}, \mathrm{m}), 1.76-1.09(8 \mathrm{H}, \mathrm{m}), 0.93(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=5.9 \mathrm{~Hz})$; MS (ESI, positive): 307 ([M+H] ${ }^{+}$, base peak), $329[\mathrm{M}+\mathrm{Na}]^{+}$.
$\alpha$-syn-\{[(S)- $\alpha$-Methylbenzyl]carbamoyl\}oximino- $\alpha$-(2-pyridyl)acetic acid 18s, yield: $80 \%$, white solid; mp $88^{\circ} \mathrm{C}$ (dec.); TLC (EA:hex = 1:2), origin spot; ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{DMSO}-\mathrm{d}_{6}$ ) $\delta 8.70(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=4.4 \mathrm{~Hz}$ ), 8.32 $(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.9 \mathrm{~Hz}), 8.14(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.8 \mathrm{~Hz}), 7.99(1 \mathrm{H}, \mathrm{m}), 7.60-7.25(5 \mathrm{H}, \mathrm{m}), 4.82(1 \mathrm{H}, \mathrm{m}), 1.48(3 \mathrm{H}, \mathrm{d}$, $\mathrm{J}=7.0 \mathrm{~Hz}$ ); MS (ESI, positive): $337[\mathrm{M}+\mathrm{H}+\mathrm{Na}]^{+}$.

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