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Rearrangement of Nitropyridylidenemalonate 1-Oxides. A Novel Method for the Synthesis of Aminopyridine Derivatives

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Abstract—Knoevenagel condensation between 3-nitro-2-pyridinecarbaldehyde and diethyl malonate catalyzed by titanium(IV) chloride gave diethyl 3-nitro-2-pyridylidenemalonate which was oxidized with peracetic acid to give corresponding 1-oxide. Reaction of the latter with diethylamine in the presence of primary and secondary alcohols resulted in the reduction of the nitro group and the oxidation of the vinylic carbon attached to the pyridine ring. Simultaneous migration of the malonic fragment gave the appropriate 3-amino-2-pyridinecarboxylate esters. The 4-nitro-3-pyridylidenemalonate 1-oxide rearranges into the corresponding 4-amino-3-pyridinecarboxylate analogue.
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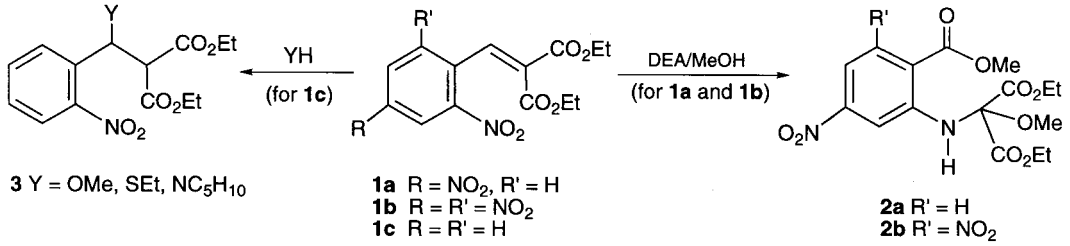
Introduction

Synthetic methods involving neighboring group interaction in *ortho*-substituted nitrobenzene derivatives have been reviewed[1,2] and new examples continue to attract interest.[3] Such redox processes usually involve an intramolecular aldol condensation of the *ortho*-substituent with the nitro group acting as the electrophilic center and have been used to synthesize a variety of heterocyclic compounds. These reactions typically occur under basic conditions with or without external reductive reagents and frequently involve thermal transformations.[1]

In previous work, we found that treatment of diethyl 2,4-dinitrobenzylidenemalonate (**1a**) with diethylamine (DEA) in MeOH did not lead to the expected Michael addition of DEA to the polarized carbon–carbon double bond. Instead it gave the 2-amino-4-nitrobenzoic acid derivative **2a**[4] (Scheme 1). Such an unusual reductive-oxidative rearrangement selectively yields a variety of products of type **2** when different primary or secondary alcohols,[4,5] thiols[6] or amines[4,5] were used instead of MeOH. The new ester, thioester or amide bond is formed at position 1, and a new ether, thioether or amine bond is formed at the C-malonate carbon, respectively. Reactivity toward rearrangement increases with an increasing number of nitro groups on the aromatic ring. It was found that the 2,4,6-trinitro compound **1b** rearranges to **2b** in all cases under the mildest conditions.[5,6] In



Scheme 1.

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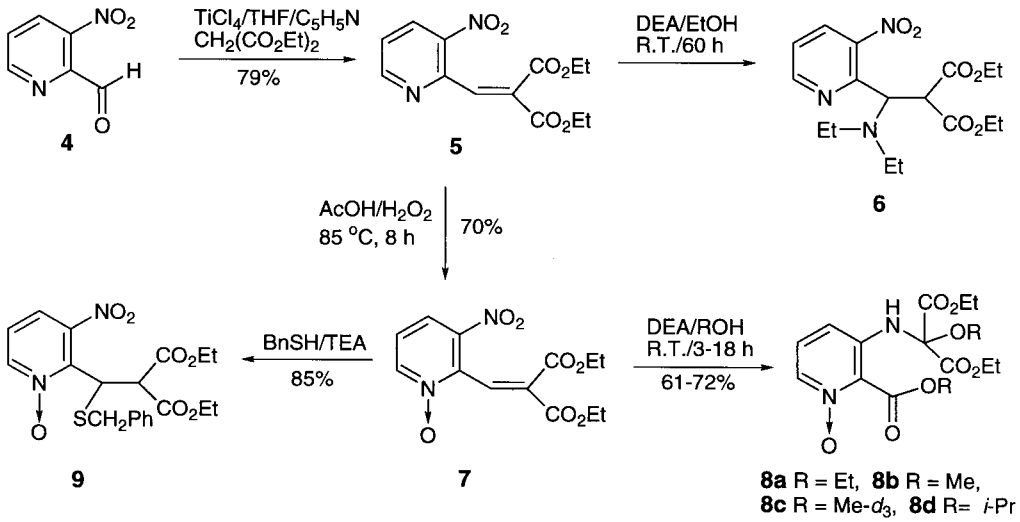


Scheme 2.

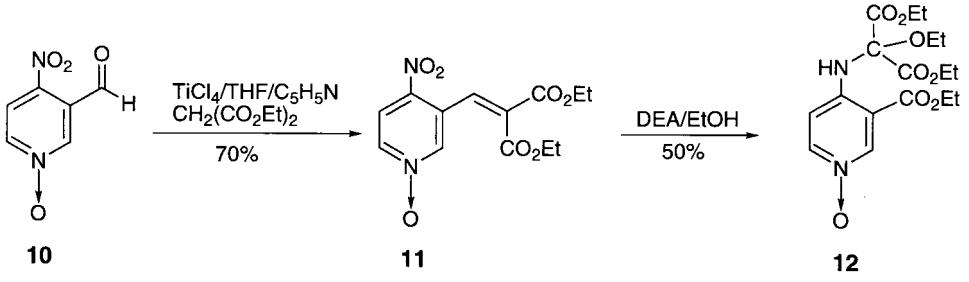
contrast, 2-nitrobenzylidenemalonate **1c** does not rearrange and forms the stable Michael type adducts **3** with amines, alkoxides, or thiolates.[4,6]

We reasoned that such skeletal rearrangement might prove effective for heterocyclic π-deficient analogues in which the electron-withdrawing role of the second nitro group on the phenyl ring would be replaced by a sp^2 hybridized nitrogen atom in the ring. Thus, appropriate nitropyridylidenemalonates bearing nitro and alkenyl substituents in the *ortho* position to each other (e.g., **7** or **11**) can undergo rearrangement to the amino-substituted pyridinecarboxylate derivatives (e.g., **8** or **12**). Aminopyridines are prepared by a variety of methods including direct nucleophilic amination (the Chichibabin reaction), cyclization of open-chain precursors,[7] and the electrophilic nitration of pyridine analogues followed by reduction.[8] It was recently discovered that 3-amino-2-pyridinecarbaldehyde thiosemicarbazone is a potent inhibitor of ribonucleoside reductase with broad spectrum antitumor activity.[9] The 4,6-disubstituted 3-cyano-2-aminopyridines show anti-inflammatory activity,[10] and the aminopyridine segments are at the core of dipyridodiazopinones-based non-nucleoside inhibitors of HIV reverse transcriptases.[11] We now report a one-step rearrangement of *ortho*-nitropyridylidenemalonates that selectively produces various amino-substituted pyridinecarboxylate derivatives.

Results and Discussion

From the possible four isomers of nitropyridine carbaldehydes with nitro and formyl substituents *ortho* to each other, we first chose 3-nitro-2-pyridinecarbaldehyde (**4**) which can be considered as an analogue of 2,6-dinitrobenzaldehyde. Aldehyde **4** was prepared by oxidation (SeO_2/dioxane) of 2-methyl-3-nitropyridine.[9a,12] Similarly to the reaction between 2,4-dinitrobenzaldehyde and diethyl malonate,[4,13] treatment of **4** with diethyl malonate in benzene in the presence of triethylamine (TEA) gave the expected β-hydroxy adduct [2,2-diethoxycarbonyl-1-(3-nitro-2-pyridyl)-ethanol]. Knoevenagel reaction of **4** with diethyl malonate catalyzed by $TiCl_4$/pyridine[14] gave *ortho*-nitropyridylidenemalonate **5** (analogue of diethyl 2,6-dinitrobenzylidenemalonate) in 79% yield (Scheme 2). However, treatment of **5** with diethylamine (DEA) in ethanol gave the stable Michael addition adduct **6** as observed with 2-nitrobenzylidenemalonates[4,6] (e.g., **1c→3**). The ^{1}H NMR spectra of **6** showed two doublets at δ 4.60 and 5.14 (J=11.3 Hz) for the methine protons, and HRMS showed molecular ion as a base peak at m/z 368.1821 (100, $MH^+[C_{17}H_{26}N_3O_6]$= 368.1822).

Oxidation of **5** gave the 1-oxide **7**, which has an even stronger electron-withdrawing effect. Treatment of **7** with DEA in EtOH (ambient temperature/4 h) gave the rearranged



Scheme 3.

product **8a** with the ethoxycarboxylate group in position 2 and a second molecule of EtOH attached to the rearranged C-malonate carbon (68% yield after silica gel purification). Analogous treatment of **7** with DEA/MeOH or MeOH-d_4 gave the corresponding 3-amino-2-pyridinecarboxylate methyl ester **8b** and **8c**. Secondary isopropanol produces the somewhat unstable **8d**. Treatment (TEA or DEA/THF) of **7** with benzyl mercaptan does not produce rearranged products[6] but instead gave the stable product **9** from the addition of the thiol to a carbon–carbon double bond.

The general utility of the rearrangement was further illustrated using 4-nitro-3-pyridinecarbaldehyde 1-oxide **10** (2,5-dinitrobenzaldehyde analogue). The unknown aldehyde **10** was prepared by treatment of 3-methyl-4-nitropyridine 1-oxide[15] with *N*,*N*-dimethylformaldehyde dimethylacetal followed by oxidative cleavage[16] of the resulting enamines with periodate (55% overall). Condensation of **10** with diethyl malonate ($TiCl_4$/pyridine[14]) gave diethyl 4-nitro-3-pyridylidenemalonates 1-oxide **11** in 70% yield after column chromatography (Scheme 3). Treatment of **11** with DEA/EtOH resulted in rearrangement and formation of the somewhat unstable 4-amino-3-pyridinecarboxylate ester **12** in 50% yield.

In summary, reaction of *ortho*-nitropyridylidenemalonate 1-oxides with diethylamine in the presence of primary or secondary alcohols produces a variety of aminopyridinecarboxylate 1-oxide derivatives. Two alcohol molecules take part in these reductive-oxidative rearrangement, one molecule is converted into an ester and the other into an ether derivative. A tentative mechanism for the analogous rearrangement on *ortho*-nitrobenzylidenemalonates has been proposed.[4] Such a redox rearrangement is assumed to proceed via an intramolecular aldol-type condensation between the nitro group or intermediate nitroso group and the C-malonate carbon.

Experimental

^{1}H NMR spectra were determined at 200 or 400 MHz, and ^{13}C spectra at 50 or 100 MHz ($Me_4Si/CDCl_3$) with solution in $CDCl_3$ unless otherwise noted. Mass spectra (MS and HRMS) were obtained with electron impact (20 eV), chemical ionization (CI, CH_4), or fast atom bombardment (glycerine matrix) techniques. TLC was performed on precoated silica gel sheets (Merck kieselgel 60-F_{254}) containing a fluorescent indicator. Silica gel 60 (230–400 mesh) was used for column chromatography. Elemental analyses were determined at microanalytical laboratories at Adam Mickiewicz University, Poznan, Poland or Galbraith Laboratories, Knoxville, TN. Reagent grade chemicals were used and solvents were dried by reflux over and distillation from CaH_2 under an argon atmosphere.

2-[(2,2-Diethoxycarbonyl)ethen-1-yl]-3-nitropyridine (5). Procedure A. Titanium(IV) chloride (1.1 mL, 10 mmol) in CCl_4 (3.0 mL) was added dropwise to anhydrous THF (40 mL) under N_2 and the stirred mixture was cooled in ice-bath. After 15 min, 3-nitro-2-pyridinecarbaldehyde[9a,12] (**4**; 0.76 g, 5 mmol) in anhydrous THF (5 mL) and diethyl malonate (0.76 mL, 0.80 g, 5 mmol) were added. After 5 min, pyridine (1.6 mL, 20 mmol) in anhydrous THF (5 mL) was added dropwise over 20 min and the dark reaction mixture was allowed to warm to ambient temperature and was stirred for 12 h. The reaction was quenched with H_2O (10 mL) and Et_2O (10 mL), the organic layer was separated and the aqueous layer extracted with Et_2O (2×15 mL). The combined organic layer was washed with brine (25 mL), saturated $NaHCO_3/H_2O$ (2×25 mL), brine (25 mL), dried ($MgSO_4$), and evaporated. The crude product was purified by column chromatography ($CHCl_3$→5% $Me_2CO/CHCl_3$) to give **5** (1.16 g, 79%) as a yellow syrup: IR (neat) ν 1731, 1632, 1591 cm^{-1}; ^{1}H NMR δ 1.21 and 1.29 (2×t, J=7.2 Hz, 2×3, 2×CH_3), 4.27 (quint, J=7.2 Hz, 4, 2×CH_2), 7.49 (dd, J=8.4, 4.7 Hz, 1, H_β), 8.12 (s, 1, CH), 8.33 (dd, J=8.4, 1.4 Hz, 1, H_γ), 8.73 (dd, J=4.7, 1.4 Hz, 1 H_α); ^{13}C NMR δ 14.4, 14.5, 61.9, 62.9, 125.3, 133.4, 135.0, 145.8, 146.5, 153.0, 163.8, 165.8. HRMS (CI) m/z calcd for $C_{13}H_{15}N_2O_6$ (MH^+): 295.0930; found 295.0930. Anal. Calcd for $C_{13}H_{14}N_2O_6$ (294.27): C, 53.06; H, 4.80; N, 9.52. Found: C, 52.97; H, 5.00; N, 9.22.

Treatment of **4** (45 mg, 0.3 mmol) with diethyl malonate (0.061 mL, 64 mg, 0.4 mmol) in benzene (5 mL) in the presence of triethylamine (13 μL, 10 mg, 0.1 mmol) at ambient temperature for 2 h and evaporation of volatiles gave mixture (~3:2) of unchanged **4** and β-hydroxy adduct [2,2-diethoxycarbonyl-1-(3-nitro-2-pyridyl)ethanol] which was characterized spectroscopically. The β-hydroxy compound had: ^{1}H NMR δ 4.12–4.29 (m, 5, CH and 2×CH_2), 6.06 (d, J=6.6 Hz, 1, CH). HRMS (CI) m/z calcd for $C_{13}H_{17}N_2O_7$ (MH^+): 313.1036; found 313.1042.

Reaction of 5 with diethylamine in EtOH. DEA (0.1 mL, 73 mg, 1.0 mmol) was added to a solution of **5** (88 mg, 0.3 mmol) in EtOH (3 mL, 99.5%) and stirring was continued at ambient temperature for 60 h. Volatiles were evaporated to give an oily residue as a mixture (~1:1) of unchanged **5** and **6** {2-[2,2-diethoxycarbonyl-1-(diethylamino)ethyl]-3-nitropyridine}. ^{1}H NMR (signals for **6** only) δ 0.81–1.42 (m, 12, 4×CH_3), 2.18–2.65 (m, 4, 2×CH_2), 3.98–4.26 (m, 4, 2×OCH_2), 4.60 (d, J=11.3 Hz, 1, CH), 5.54 (d, J=11.3 Hz, 1, CH), 7.33 (dd, J=8.2, 4.8 Hz, 1, H_β), 8.08 (dd, J=8.3, 1.5 Hz, 1, H_γ), 8.63 (dd, J=4.8, 1.5 Hz, 1, H_α). HRMS (CI) m/z calcd for $C_{17}H_{26}O_6N_3$ (MH^+, **6**): 368.1822; found 368.1821.

2-[2,2-Diethoxycarbonyl)ethen-1-yl]-3-nitropyridine 1-oxide (7). Hydrogen peroxide (50%, 3 mL) was added to a solution of **5** (500 mg, 1.7 mmol) in glacial AcOH (8 mL) and the resulting mixture was heated at 80°C for 4 h. TLC ($CHCl_3$/MeOH, 9:1) indicated ~50% conversion to a more polar product. New portions of AcOH (4 mL) and H_2O_2 (2 mL) were added and heating was continued for an additional 4 h. Volatiles were evaporated, and the residue was partitioned ($NaHCO_3/H_2O/CHCl_3$). The organic phase was washed (brine), dried ($MgSO_4$) and evaporated. Column chromatography (50→95% EtOAc/hexane) gave unchanged **5** (80 mg, 16%) and **7** (370 mg, 70%) as a yellow syrup: IR (neat) ν 1721, 1538, 1266, 1213 cm^{-1}; ^{1}H NMR δ 1.19 and 1.37 (2×t, J=7.2 Hz, 2×3, 2×CH_3), 4.16 and 4.36 (2×q, J=7.2 Hz, 2×2, 2×CH_2), 7.43 (dd, J=8.4, 6.6 Hz, 1, H_β), 7.75 (s, 1, CH), 7.90 (d, J=8.4 Hz, 1, H_γ), 8.42 (d, J=6.6 Hz, 1, H_α); ^{13}C NMR δ 14.3, 14.5, 62.4, 62.7,

120.9, 125.4, 133.3, 141.4, 142.5, 143.8, 148.2, 163.4. HRMS (CI) *m/z* calcd for $C_{13}H_{15}N_2O_7$ (MH^+): 311.0879; found 311.0888. Anal. Calcd for $C_{13}H_{14}N_2O_7 \cdot 0.5$EtOAc (354.34): C, 50.85; H, 5.12; N, 7.91. Found: C, 50.52; H, 5.31; N, 7.61.

Ethyl 3-[(diethoxycarbonyl)(ethoxy)methyl]amino-2-pyridinecarboxylate 1-oxide (8a). Procedure B. Compound **7** (62 mg, 0.2 mmol) was dissolved in EtOH (2 mL, 99.5%) and DEA (10 μL, 7.3 mg, 0.1 mmol) was added at ambient temperature. After 4 h, volatiles were evaporated and the residue was column chromatographed (50→95% EtOAc/hexane or $CHCl_3$→2% MeOH/$CHCl_3$) to give **8a** (52 mg, 68%) as a yellow syrup: IR (neat) ν 3383, 1742, 1591, 1275 cm^{-1}; ^1H NMR δ 1.22–1.31 (m, 9, 3×CH_3), 1.48 (t, J=7.1 Hz, 3, CH_3), 3.48 (q, J=7.1 Hz, 2, CH_2), 4.30 (q, J=7.1 Hz, 4, 2×CH_2), 4.59 (q, J=7.2 Hz, 2, CH_2), 7.10–7.22 (m, 2, H_β and H_γ) 7.88 (br d, J=5.8 Hz, 1, H_α), 9.51 (br s, 1, NH); ^{13}C NMR δ 14.4, 14.5, 15.3, 60.1, 63.5, 63.8, 87.5, 112.9, 127.3, 129.9, 132.6, 142.1, 163.5, 166.1. HMRS (CI)*m/z* calcd for $C_{17}H_{24}N_2O_8$ (MH^+): 385.1611; found 385.1599. Anal. Calcd for $C_{17}H_{24}N_2O_8$ (384.39): C, 53.12; H, 6.29; N, 7.29. Found: C, 53.55; H, 6.01; N, 7.59.

Methyl 3-[(diethoxycarbonyl)(methoxy)methyl]amino-2-pyridinecarboxylate 1-oxide (8b). Treatment of **7** (47 mg, 0.15 mmol) by procedure B (DEA/MeOH) gave **8b** (35 mg, 69%) as a yellow solidifying syrup: IR (neat) ν 3382, 1744, 1593, 1264 cm^{-1}; ^1H NMR δ 1.25 (t, J=7.1 Hz, 6, 2×CH_3), 3.30 (s, 3, CH_3) 4.10 (s, 3, CH_3), 4.31 (q, J=7.1 Hz, 4, 2×CH_2), 7.07–7.14 (m, 2, H_β and H_γ), 7.83 (dd, J=4.9, 1.6 Hz, 1, H_α), 9.59 (br s, 1, NH); ^{13}C NMR δ 14.4 51.7, 53.9, 63.9, 88.0, 112.8, 127.3, 129.8, 132.6, 142.2, 163.5, 166.1. HRMS *m/z* calcd for $C_{15}H_{20}N_2O_8$ (M^+): 356.1220; found 356.1203.

Methyl-d_3 3-[(diethoxycarbonyl)(methoxy-d_3)methyl]-amino-2-pyridinecarboxylate 1-oxide (8c). Treatment of **7** (47 mg, 0.15 mmol) by procedure B (3 h, DEA/MeOH-d_4) gave **8c** (39 mg, 72%) with spectroscopic data corresponded to those for **8b** except for the missing signals at δ 3.30 and 4.10 (^1H NMR) and δ 51.7, 53.9 (^{13}C NMR). HRMS (CI) *m/z* calc for $C_{15}H_{15}D_6N_2O_8$ (MH^+): 356.1675; found 353.1664.

Isopropyl 3-[(diethoxycarbonyl)(isopropoxy)methyl]-amino-2-pyridinecarboxylate 1-oxide (8d). Treatment of **7** (78 mg, 0.25 mmol) by procedure **B** (18 h, DEA/*i*-PrOH) gave **8d** (63 mg, 61%) as a yellow syrup contaminated by other product(s) (~5–10%, ^1H NMR): ^1H NMR δ 1.10–1.48 m, 18, 6×CH_3), 3.91 (septet, J=6.1 Hz, 1, CH), 4.28 (q, J=7.1 Hz, 4, 2×CH_2), 5.42 (septet, J=6.1 Hz, 1, CH), 7.10–7.24 (m, 2, H_β and H_γ), 7.85 (br d, J=5.8 Hz, 1, H_α), 9.60 (br s, 1, NH). HRMS (CI) *m/z* calcd for $C_{19}H_{29}N_2O_8$ (MH^+): 413.1924; found 413.1939.

2-[2,2-Diethoxycarbonyl-1-(benzylthio)ethyl]-3-nitro-pyridine 1-oxide (9). Phenylmethanethiol (0.18 mL, 188 mg, 1.5 mmol) and TEA (21 μL, 15 mg, 0.15 mmol) were added to a solution of **7** (93 mg, 0.3 mmol) in anhydrous THF (3 mL) and stirring was continued at ambient temperature overnight. TLC (EtOAc/MeOH, 12:1) indicated ~90% conversion to a less polar product. Volatiles were evaporated, and the residue was flash chromatographed (EtOAc→2% MeOH/EtOAc) to give **9** (111 mg, 85%) as a yellow syrup: IR (neat) ν 1727, 1535 cm^{-1}; ^1H NMR δ 1.09 and 1.35 (2×t, J=7.1 Hz, 2×3, 2×CH_3), 3.88 (d, J=12.5 Hz, 1, SCH_2), 3.98 (q, J=7.1 Hz, 2, CH_2), 4.06 (d, J=12.5 Hz, 1, SCH_2), 4.32 (q, J=7.1 Hz, 2, CH_2), 4.91 (d, J=11.1 Hz, 1, CH), 5.13 (d, J=11.1 Hz, 1 CH), 7.18–7.32 (m, 6, H_{arom} and H_β), 7.63 (d, J=8.2 Hz, 1, H_γ), 8.30 (d, J=6.1 Hz, 1, H_α); ^{13}C NMR δ 14.3, 14.7, 39.8, 42.0, 53.8, 62.4, 121.5, 123.6, 127.8, 129.0, 129.5, 137.7, 143.2, 147.1, 147.8, 167.8, 168.0. HRMS (CI) *m/z* calcd for $C_{20}H_{23}N_2O_7S$ (MH^+): 435.1226; found 435.1213. Anal. Calcd for $C_{12}H_{22}N_7O_7S$ (434.48): C, 55.29; H, 5.10; N, 6.45. Found: C, 55.64; H, 5.29; N, 6.30.

Analogous treatment of **7** (31 mg, 0.1 mmol) with phenylmethanethiol (0.06 mL, 62 mg, 0.5 mmol) using DEA (5 μL, 4 mg, 0.05 mmol) instead of TEA gave **9** (36 mg, 83%).

4-Nitro-3-pyridinecarbaldehyde 1-oxide (10). *N,N*-Dimethylformaldehyde dimethylacetal (3.98 mL, 3.57 g, 30 mmol) was added dropwise to a solution of 3-methyl-4-nitropyridine 1-oxide[15] (1.54 g, 10 mmol) in DMF (10 mL) under N_2. The solution was heated at 140°C for 90 min and was allowed to cool. The dark-violet precipitate formed was filtered to give intermediate enamine[16] [1.8 g, 86%; mp 180–182°C; ^1H NMR δ 6.01 (d, J=13.5 Hz, 1, CH), 7.15 (d, J=13.5 Hz, 1, CH)]. This enamine (1.5 g, 7.2 mmol) and $NaIO_4$ (4.62 g, 21.6 mmol) were dissolved in THF/H_2O (1:1, 50 mL) and stirring was continued at ambient temperature for 12 h. The insolubles ($NaIO_3$) were filtered and the filtrate was washed with EtOAc (4×20 mL). The combined organic phase was washed with $NaHCO_3$/H_2O, dried ($MgSO_4$) and volatiles were evaporated to give **9** (774 mg, 64%) as a yellow crystal: mp 162°C (dec.); IR (KBr) ν 1701 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.23 (d, J=7.0 Hz, 1, H_β), 8.47 (d, J=2.0 Hz, 1, H_α), 8.57 (dd, J=7.0, 2.0 Hz, 1, H_α), 10.26 (s, 1, CHO); ^{13}C NMR (DMSO-d_6) δ 122.4, 130.2, 139.0, 142.1, 142.5, 187.4. HRMS *m/z* calcd for $C_6H_4N_2O_4$ (M^+): 168.0171; found 168.0162. Anal. Calcd for $C_6H_4N_2O_4$ (168.11): C, 42.87; H, 2.40; N, 16.66. Found: C, 42.56; H, 2.67; N, 16.81.

3-[(2,2-Diethoxycarbonyl)ethen-1-yl]-4-nitropyridine 1-oxide (11). Treatment of **10** (0.5 g, 3 mmol) by procedure A [column chromatography: $CHCl_3$/CCl_4 (2:1)→$CHCl_3$/CCl_4/MeOH (9:5:1)] gave **11** (650 mg, 70%) as a syrup: IR ($CHCl_3$) ν 1731, 1241 cm^{-1}; ^1H NMR δ 1.23 and 1.36 (2×t, J=7.1 Hz, 2×3, 2×CH_3), 4.21 and 4.35 (2×q, J=7.1 Hz, 2×2, 2×CH_2), 7.97 (s, 1, CH), 8.12–8.15 (m, 2, $H_{\alpha,\beta}$), 8.27 (dd, J=7.1, 1.6 Hz, 1, H_α); ^{13}C NMR δ 14.0, 14.1, 62.2, 62.5, 121.8, 129.5, 131.6, 134.9, 135.3, 139.0, 139.6, 162.3, 163.3. HRMS (FAB) *m/z* calc for $C_{13}H_{15}N_2O_7$ (MH^+): 311.0879; found 311.0875. Anal. Calcd for $C_{13}H_{14}N_2O_7$ (310.27): C, 50.32; H, 4.55; N, 9.03; Found: C, 50.47; H, 4.86; N, 8.81.

Ethyl 4-[(diethoxycarbonyl)(ethoxy)methyl]amino-3-pyridinecarboxylate 1-oxide (12). Treatment of **11** (79 mg, 0.25 mmol) by procedure B (6 h, DEA/EtOH) gave **12** (48 mg, 50%) as a yellow syrup: IR ($CHCl_3$) ν

3350, 1745, 1711, 1219 cm^{-1}; ^1H NMR δ 1.20–1.29 (m, 9, 3×CH_3), 1.40 (t, J=7.1 Hz, 3, CH_3), 3.43 (q, J=7.1 Hz, 2, CH_2), 4.28–4.37 (m, 4H, 2×CH_2), 4.43 (q, J=7.1 Hz, 2, CH_2), 7.18 (d, J=7.0 Hz, 1, H_β), 8.05 (dd, J=7.0, 2.0 Hz, 1, H_α), 8.77 (d, J=2.0 Hz, 1, H_α), 9.80 (br s, 1, NH); ^{13}C NMR δ 13.9, 14.0, 14.8, 60.0, 62.2, 63.5, 63.6, 86.7, 111.5, 111.6, 140.9, 142.9, 144.4, 164.8, 165.4, 165.7. HRMS *m/z* calcd for $C_{17}H_{24}N_2O_8$ (M^+): 384.1533; found 384.1504. Anal. Calcd for $C_{17}H_{24}N_2O_8$ (384.39): C, 53.12; H, 6.29; N, 7.29. Found: C, 53.48; H, 6.01; N, 7.01.

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