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Research Article

The ^{14}C, ^{13}C and ^{15}N syntheses of MON 37500, a sulfonylurea wheat herbicide

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Summary
[^{14}C] and [^{13}C]MON 37500 labeled in the imidazopyridine (Im) ring system were synthesized in seven steps in an overall yield of 39 and 28%, respectively, from [2-^{14}C] and [2-^{13}C]chloroacetic acid. [^{14}C]MON 37500 labeled in the pyrimidine (Pd) ring system was synthesized from [2-^{14}C]diethyl malonate in four steps in 48% yield. Lastly, [^{15}N]MON 37500 was prepared in three steps in an overall yield of 28% from [^{15}N]ammonium chloride. Copyright © 2005 John Wiley & Sons, Ltd.

Key Words: sulfonylurea; wheat herbicide; MON 37500; Maverick®; Monitor®

Introduction
MON 37500 or sulfosulfuron is a sulfonylurea herbicide co-developed by Monsanto Company and Takeda Chemical Industries, Ltd. under the brand names *Monitor®* in Europe and *Maverick®* in the US.[1] It has been found to effectively control several grassy weeds in wheat. The mode of action involves the inhibition of acetolactate synthase, an enzyme in the biosynthesis of essential amino acids leucine, valine and isoleucine.[2] To complete environmental plant, animal, soil and water studies for registration, the syntheses of [^{14}C], [^{13}C] and [^{15}N]MON 37500 were required. Material radiolabeled in both ring systems was required in order to follow the metabolism of each ring system. Stable labels were required to make identification of metabolites easier by NMR and MS. This paper describes the radiolabel and stable label syntheses and analysis of the active ingredient, MON 37500, in Monitor® and Maverick® herbicides.

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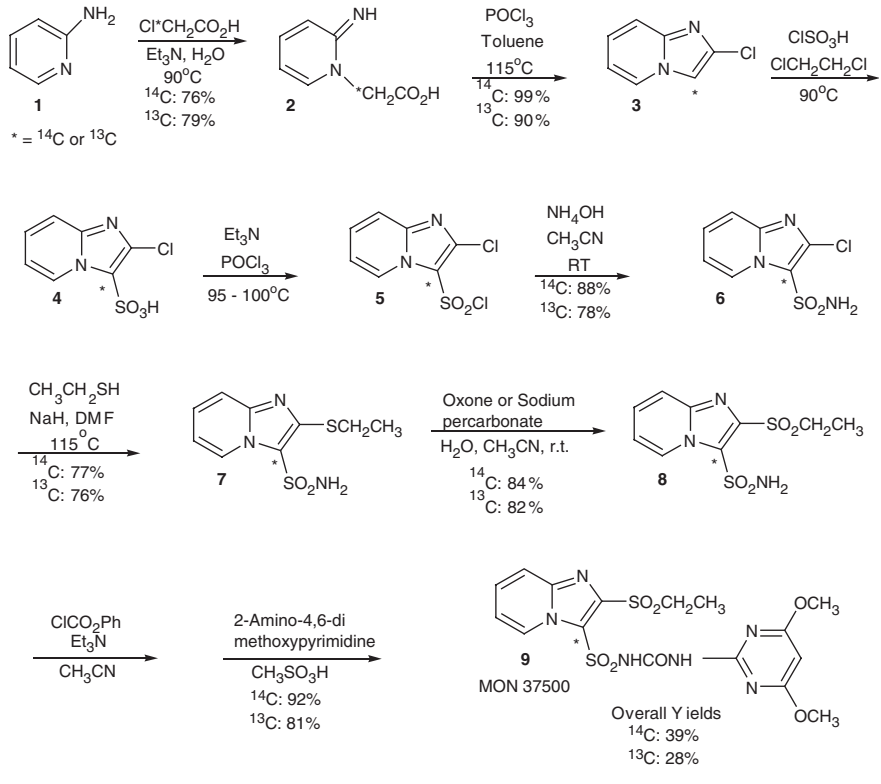
Results and discussion

Four separate labeled compounds were synthesized according to the routes illustrated in Schemes 1–3. In Scheme 1 is shown the synthesis of [^{14}C] and [^{13}C]MON 37500 labeled in the imidazopyridine (Im) ring system. The label was introduced by reacting [2-^{14}C] or [2-^{13}C]chloroacetic acid with 2-aminopyridine to generate product **2**. Substituted acetic acid **2** was cyclized to the chloroimidazopyridine **3** in excellent yield.[3] Product **3** was converted to the sulfonic acid and then to the acid chloride in a single flask with chlorosufonic acid and phosphorous oxychloride. Addition of ammonia to the acid chloride formed amide **6** in good yield for the three steps. Chloroamide **6**[4] was converted to sulfide **7**[5] which was oxidized to the sulfone using sodium percarbonate for the ^{13}C synthesis and Oxone® for the ^{14}C synthesis. We found that the sodium percarbonate lost activity over time and the Oxone® worked as well without decomposition. The final step involved the reaction of product **8** with phenyl chloroformate to form the carbonyl portion of the sulfonylurea bridge followed by the attachment of 2-amino-4,6-dimethoxypyrimidine.[6] Overall yields were 39 and 28% for the ^{14}C and ^{13}C syntheses, respectively.



Scheme 1.

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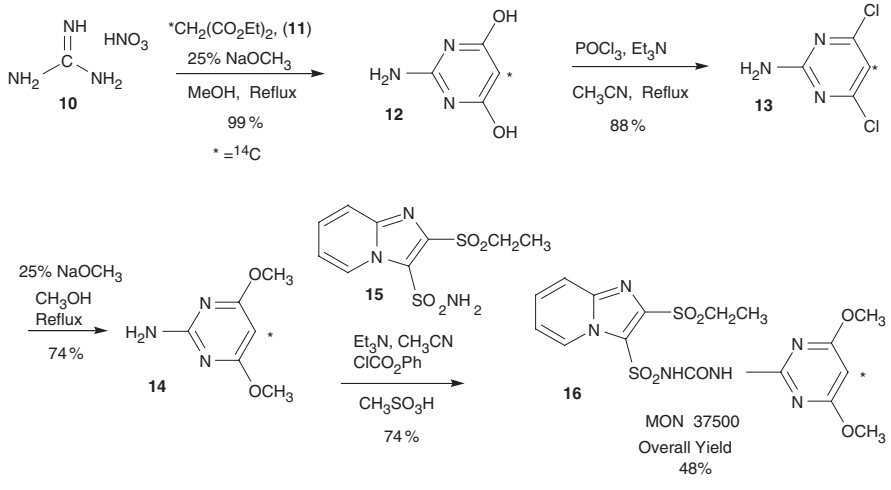
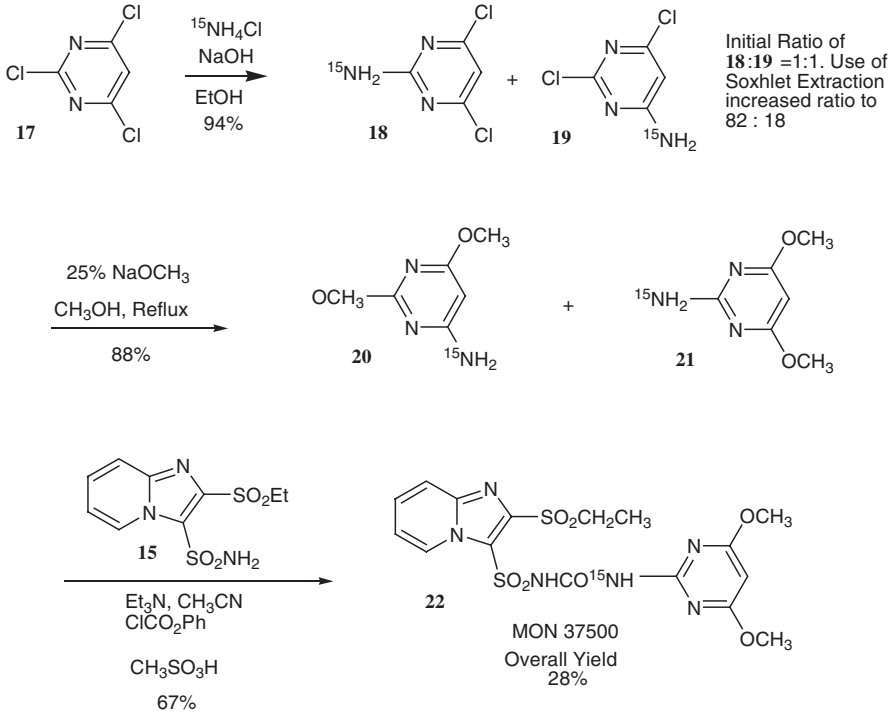
Scheme 2 shows the synthesis of [^{14}C-Pd]MON 37500. Guanidine nitrate was reacted with [2-^{14}C]diethyl malonate and 25% NaOMe in MeOH to form 2-amino-4,6-[5-^{14}C]dihydroxypyrimidine **12** in 99% yield. Product **12** was



Scheme 2.



Scheme 3.

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converted to the dichloride **13** in 88% yield with $POCl_3$ and Et_3N in refluxing MeCN. The dichloride was reacted with 25% NaOMe in refluxing MeOH to produce 2-amino-4,6-[5-^{14}C]dimethoxypyrimidine **14** in 74% yield. Product **14** was reacted under the same conditions for the last step described in Scheme 1 to give [^{14}C-Pd]MON 37500 in 74% yield.[6] The overall yield for the four steps was 48%.

[^{15}N]MON 37500 was prepared as shown in Scheme 3. The label was introduced by condensing $^{15}NH_3$ generated from solid $^{15}NH_4Cl$ and NaOH into EtOH. To this was added trichloropyrimidine, **17**. An equal mixture of regioisomers **18** and **19** was formed. The ratio of products was determined by integrating the ^{1}H-NMR signal for the protons attached to C5 of products **18** and **19**. The chemical shift of the C5 proton in product **18** appears at 6.88 ppm and that of product **19** appears at 6.46 ppm. The mixture of the two regioisomers was placed in a Soxhlet Extractor and was refluxed with benzene overnight. This increased the ratio of products 18/19 to 82/18. This mixture was reacted with 25% NaOMe in MeOH at reflux to give the two isomeric dimethoxypyrimidines **20** and **21** which were separated by flash column chromatography. Product **21** was reacted with phenyl chloroformate and product **15** to give [^{15}N]MON 37500 in 67% yield for the last step.[6] The overall yield for the three step synthesis was 28%.

Experimental

Radioactivity was determined using Tracor Analytic Mark III counters, which were interfaced with a Monsanto developed software package. Flash column chromatography was performed using Merck grade silica gel, 230–400 mesh. HPLC analysis was performed using a Waters HPLC system consisting of a model 680 gradient controller, two model 510 pumps, a model U6 K injector, a model 481 UV detector set at 254 nm, a Packard Radiomatic Flo-One Beta radioactivity detector, and a Beckman Ultrasphere column, C18, 5 μm, 4.6 × 250 mm. Proton NMR was completed on a Varian 300 MHz instrument and chemical shifts were referenced against TMS. GC-CIMS and DEP-CIMS analyses were completed on a Finnigan model 4515 instrument using isobutane. Electrospray MS was performed on a Finnigan 4535 quadrupole mass spectrometer with a Vestec Model 601B electrospray interface. LC-FAB MS was completed using a VG ZAB-HF double-focusing MS via a dynamic FAB probe. All labeled materials were identified by HPLC, TLC, MS and NMR comparison with the corresponding unlabeled materials.

[^{14}C-Im]MON 37500

[2-^{14}C]2-(2-Imino-1,2-dihydropyridin-1-yl)acetic acid, **2**. To [2-^{14}C]chloroacetic acid (1.84 g, 19.4 mmol, 605 mCi, specific activity = 31 mCi/mmol, NEN, Boston, MA) in water (3 ml) was added Et_3N (3.1 ml, 22 mmol) dropwise at

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room temperature (RT). After stirring for 10 min, 2-aminopyridine **1** (2.2 g, 23 mmol) was added and the resulting brown solution was warmed to 90°C for 5 h. After cooling to RT, EtOH (2 ml) was added and the suspension was stirred at 5°C for 2 h. The precipitate was collected by filtration and rinsed with cold EtOH and dried under vacuum at RT for 24 h to produce 2.24 g (76% yield) of product **2**.

[3-^{14}C]2-Chloroimidazo[1,2-a]pyridine, **3**.[3] To **2** (2.24 g, 14.7 mmol) in toluene (10 ml) at reflux was added $POCl_3$ (4.1 ml, 44 mmol) dropwise. After refluxing for 16 h and cooling to RT, cold water (50 ml) was added and the solution was stirred for 15 min. The layers were separated. In an ice bath, the aqueous layer was neutralized with 10% NaOH (aq). The precipitate was filtered, dissolved in CH_2Cl_2 (50 ml) and dried over Na_2SO_4. The aqueous filtrate was extracted with CH_2Cl_2 (20 ml × 4). The combined organic layers were washed with brine and dried over Na_2SO_4. The two CH_2Cl_2 solutions were filtered, combined and the solvent was removed by rotary evaporation to give 4.7 g of a yellow powder. This material was purified by flash column chromatography on silica using 60% EtOAc/40% Hexane resulting in 2.23 g (99%) of **3** as white crystals. TLC analysis produced a single spot with an R_f of 0.70 when co-spotted with reference material on silica using 60% EtOAc/40% hexane.

[3-^{14}C]2-Chloroimidazo[1,2-a]pyridine-3-sulfonamide, **6**.[4] To **3** (2.19 g, 14.3 mmol) in DCE (20 ml) was added a solution of $ClSO_3H$ (1.7 ml, 26 mmol) in DCE (8 ml). The solution was warmed to 90°C for 5.5 h to produce **4**. Et_3N (3.8 ml, 27 mmol) was added, refluxed for 15 min, $POCl_3$ (2.53 ml, 27 mmol) was added dropwise and the solution refluxed for 5 h. After cooling in an ice water bath, cold water (60 ml) was added and the mixture was vigorously stirred. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (100 ml × 2). The combined organic phases were dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation to give **5** which was dissolved in 30 ml MeCN. To this solution at 5°C was added aqueous 28% NH_4OH (4 ml). The solution was warmed to RT overnight. The solvent was partially removed and water (20 ml) was added. The suspension was stirred in an ice water bath, filtered, washed with cold water (10 ml) and dried under high vacuum to give 2.24 g of off-white crystals. Analysis by TLC showed a single spot, $R_f = 0.40$, on silica using 60% EtOAc/40% hexane. Additional crops of crystals were recovered (440 mg) and extraction of the filtrate with EtOAc produced an additional 170 mg of product. The 610 mg of **6** were purified by flash chromatography on silica gel using 60% EtOAc/40% hexane to produce 510 mg of product **6** as white crystals. A total of 2.75 g of product **6** (88% yield) was obtained.

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[3-^{14}C]2-Ethylthioimidazo[1,2-a]pyridine-3-sulfonamide, **7**.[5] To NaH (1.51 g, 63.1 mmol) and DMF (15 ml) in an ice water bath was added EtSH (4.70 ml, 63.1 mmol) dissolved in DMF (5 ml) dropwise. The solution was warmed to RT and stirred for 1.3 h. Product **6** (2.75 g, 12.6 mmol) in DMF (5 ml) was added dropwise. The mixture was stirred at 115°C for 14 h, cooled to RT, poured into water (250 ml) and acidified with HCl to pH = 1. The aqueous layer was extracted with CH_2Cl_2 (100 ml × 4). The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation to give 2.85 g of a yellow powder. Recrystallization from EtOAc produced 2.5 g (77% yield) of product **7** as white crystals. Analysis by TLC on silica with EtOAc gave a single spot with an $R_f = 0.80$ when co-spotted with reference material. At this stage, 0.6 g of product **7** was removed to serve as a standard for future metabolism studies.

[3-^{14}C]2-Ethylsulfonylimidazo[1,2-a]pyridine-3-sulfonamide, **8**. To **7** (1.9 g, 7.4 mmol) in MeCN (100 ml) in an ice water bath was added dropwise a solution of Oxone® (19.3 g, 31.4 mmol) in 100 ml of water. The suspension was stirred at RT for 16 h and water (100 ml) and CH_2Cl_2 (100 ml) were added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (100 ml × 3). The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation to give 1.9 g of **8**. This material was dissolved in EtOAc (150 ml) with gentle heating and was passed through a short column of silica gel. Removal of the solvent by rotary evaporation produced 1.8 g (84% yield) of white crystals.

[3-^{14}C]N-[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]-2-(ethylsulfonyl)-imidazo[1,2-a]pyridine-3-sulfonamide, **9**.[6] Phenyl chloroformate (0.97 ml, 7.7 mmol) in MeCN (5 ml) was added dropwise to a solution of **8** (1.8 g, 6.4 mmol) and Et_3N (2.06 ml, 14.8 mmol) in MeCN (22 ml) in a saltwater ice bath at −5°C at a rate such that the reaction temperature remained below 10°C. The reaction mixture was warmed to RT and stirred for 1 h. In one portion, 2-amino-4,6-dimethoxypyrimidine (1.5 g, 9.7 mmol) was added and the mixture was warmed to 55°C. CH_3SO_3H (0.63 ml, 9.7 mmol) in MeCN (5 ml) was added dropwise. The white product precipitated from solution after 1.5 h. The precipitate was filtered, washed with cold water (5 ml) and dried under high vacuum to give 2.11 g of **9** as a white crystalline material. The filtrate was added to 100 ml of water and then was extracted with CH_2Cl_2 (80 ml × 3). The organic layers were combined, washed with brine and dried over Na_2SO_4. Filtration and evaporation of the solvent produced a residue that was dissolved in EtOAc. Upon standing, the 2-amino-4,6-dimethoxypyrimidine precipitated and was removed by filtration. The filtrate was purified by flash column chromatography. The product was eluted first with 60% EtOAc/

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40% hexane and then with CH_2Cl_2 followed by 90% CH_2Cl_2/10% MeOH to provide 700 mg of additional product. The final material was recrystallized from MeCN to give 2.7 g (92% yield) of white crystalline product. The radiochemical purity was determined to be 99.8% by HPLC and the specific activity (SA) was measured gravimetrically to be 30.5 mCi/mmol. Co-spotting of the product with MON 37500 standard on silica using 90% CH_2Cl_2/10% MeOH produced a single spot with an R_f value of 0.40. MS analysis by FAB (−) ion produced the expected ion clusters at $m/z = 469/471$ and by electrospray (+) ion produced the expected ion clusters at $m/z = 471/473$. ^{1}H-NMR (300 MHz, DMSO-D_6) δ 13.14 (s, 1 H, N-H); 10.76 (s, 1 H, N-H); 9.19 (d, $J = 7.1$ Hz, 1 H, Ar-H); 7.99 (d, $J = 9.1$ Hz, 1 H, Ar-H); 7.80 (t, $J = 8.0$ Hz, 1 H, Ar-H); 7.49 (t, $J = 7.1$ Hz, 1 H, Ar-H); 6.00 (s, 1 H, Ar-H); 3.95 (s, 6 H, OCH_3); 3.60 (q, $J = 7.4$ Hz, 2 H, CH_2); 1.16 (t, $J = 7.4$ Hz, 3 H, CH_3).

[^{13}C-Im]MON 37500

The synthesis of [^{13}C-Im]MON 37500 was completed using the same reaction conditions as that used in the preparation of [^{14}C-Im]MON 37500 with two minor differences. First, the ^{13}C synthesis was completed on a larger scale than that of the ^{14}C synthesis. The ^{13}C synthesis began with 12.5 g of [2-^{13}C] chloroacetic acid (99.1% ^{13}C enriched, Isotec Inc., Miamisburg, OH). Second, the oxidation of **7** to **8** in the ^{13}C synthesis, used sodium percarbonate whereas Oxone® was used in the ^{14}C synthesis. The overall yield for the preparation of the ^{13}C material was 28% and the chemical purity was 99.9% by HPLC. The melting point of the ^{13}C material was 196–198°C (reference MP = 197–199°C). Direct probe CIMS showed a molecular ion at $m/z = 472$ as expected for [^{13}C-Im]MON 37500. ^{1}H-NMR (300 MHz, DMSO-D_6) δ 13.14 (s, 1 H, N-H); 10.76 (s, 1 H, N-H); 9.19 (d, $J = 7.1$ Hz, 1 H, Ar-H); 7.99 (d, $J = 9.1$ Hz, 1 H, Ar-H); 7.80 (t, $J = 8.0$ Hz, 1 H, Ar-H); 7.49 (t, $J = 7.1$ Hz, 1 H, Ar-H); 6.00 (s, 1 H, Ar-H); 3.95 (s, 6 H, OCH_3); 3.60 (q, $J = 7.4$ Hz, 2 H, CH_2); 1.16 (t, $J = 7.4$ Hz, 3 H, CH_3). ^{13}C-NMR (300 MHz, DMSO-D_6) δ 104.8.

[^{14}C-Pd]MON 37500

[4-^{14}C]2-Amino-4,6-dihydroxypyrimidine, **12**. To guanidine nitrate, **10** (1.25 g, 10.2 mmol) in 7 ml EtOH was added [2-^{14}C]diethyl malonate **11** (1.65 g, 10.2 mmol, 600 mCi, SA = 58.5 mCi/mmol, NEN, Boston, MA) and 4.7 ml 25% NaOMe in MeOH. The solution was refluxed for 3.5 h. After cooling, the solvent was removed by rotary evaporation. The resulting solid was dissolved in 10 ml water and was neutralized with glacial AcOH. The resulting solid was filtered, washed with cold water and dried under vacuum at 60°C to give 1.31 g of product **12** (99% yield) as an off-white powder.

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[4-^{14}C]2-Amino-4,6-dichloropyrimidine, **13**. To [4-^{14}C]2-amino-4,6-dihydroxypyrimidine **12** (1.31 g, 10.1 mmol) in 6 ml MeCN was added Et_3N (2.86 ml, 20.5 mmol) followed by the dropwise addition of $POCl_3$ (1.97 ml, 21.1 mmol). The solution was refluxed for 1 h, cooled to RT and poured into ice water. The resulting brown solid was filtered and rinsed with cold water. The combined crops were dried under vacuum with mild heating to give 1.49 g of product **13** (88% yield) as a brown powder.

[4-^{14}C]2-Amino-4,6-dimethoxypyrimidine, **14**. To the [4-^{14}C]2-amino-4,6-dichloropyrimidine **13** (1.49 g, 9.00 mmol) in 6.8 ml MeOH was added 25% NaOMe in MeOH (6.16 ml, 26.9 mmol) dropwise over 15 min. The solution was refluxed for 4 h, cooled and the MeOH was removed by rotavap. The solid was washed with 9 ml of water and was filtered. Additional crops of product were recovered from the water washes. The combined crops were dried under vacuum at 50°C to produce 1.04 g of product **14** (74% yield).

N-[[4,6-Dimethoxy-2-pyrimidinyl-[5-^{14}C])amino]carbonyl]-2-(ethylsulfonyl)-imidazo[1,2a]pyridine-3-sulfonamide, **16**.[4] To a flame dried flask containing 2-ethylsulfonylimidazo[1,2*a*]pyridine-3-sulfonamide **15** (1.93 g, 6.68 mmol) was added 7 ml MeCN and Et_3N (1.87 ml, 13.4 mmol). The solution was cooled to 3°C with an ice water bath. To the reaction was added phenyl chloroformate (0.86 ml, 6.85 mmol) in 1.6 ml MeCN dropwise over 20 min keeping the temperature at 3–5°C. After the addition was complete, the solution was stirred at 3°C for 25 min and then warmed to RT and stirred for 1 h. To the reaction was added [4-^{14}C]2-amino-4,6-dimethoxypyrimidine **14** (1.04 g, 6.64 mmol). After 2 min, the solution was warmed to 55°C with an oil bath and CH_3SO_3H (0.43 ml, 6.63 mmol) in 1.6 ml MeCN was added dropwise keeping the temperature between 50 and 55°C. The reaction mixture was stirred at 50–55°C for 45 min, cooled in an ice water bath for 1.5 h and the resulting beige solid product was filtered. The solid was rinsed with cold MeCN, cold water and was dried under vacuum to give 2.31 g, 286 mCi (74% yield) of product **16**. The overall yield was 48%. The SA of **16** was measured gravimetrically to be 58.5 mCi/mmol. MS analysis using LC-FAB (–) ion produced a molecular ion at $m/z = 471$. ^{1}H-NMR (300 MHz, DMSO-D_6) δ 13.13 (s, 1 H, N-H); 10.77 (s, 1 H, N-H); 9.19 (d, $J = 7.1$ Hz, 1 H, Ar-H); 7.99 (d, $J = 9.0$ Hz, 1 H, Ar-H); 7.80 (t, $J = 8.0$ Hz, 1 H, Ar-H); 7.49 (t, $J = 7.1$ Hz, 1 H, Ar-H); 6.00 (s, 1 H, Ar-H); 3.95 (s, 6 H, OCH_3); 3.60 (q, $J = 7.4$ Hz, 2 H, CH_2); 1.16 (t, $J = 7.4$ Hz, 3 H, CH_3).

[^{15}N]MON 37500

[2-^{15}N]2-Amino-4,6-dichloropyrimidine, **18** *and [4-^{15}N]4-Amino-2,6-dichloropyrimidine,* **19**. To a flask equipped with a dry ice condenser was added EtOH (60 ml) at –78°C. NaOH (18.0 g, 450 mmol) and $^{15}NH_4Cl$ (12.6 g, 231 mmol,

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99.3% ^{15}N, Isotec Inc., Miamisburg, OH) were ground in separate mortars. The resulting powders were placed together in a flask that was connected to the dry ice condenser via tubing. Upon intermittent shaking, the $^{15}NH_3$ gas was condensed into the EtOH. After 45 min, no additional $^{15}NH_3$ was generated. The reaction was warmed to 5°C and a solution of 2,4,6-trichloropyrimidine **17** in EtOH (6 ml) was added. The temperature of the reaction increased to 50°C over 30 min and then was cooled to RT over 45 min. The precipitate was filtered, washed with water and dried to give 11.5 g (94% yield) of a white powder as a 50/50 mixture of **18** and **19** as determined by ^{1}H-NMR by integration of the protons attached to C5. The mixture was enriched in the desired isomer, **18** by Soxhlet Extraction with 250 ml of benzene for 22 h. The white precipitate that formed in the benzene solution after cooling to RT was filtered to give 5.66 g. ^{1}H-NMR analysis showed the material to be 82% of the desired [2-^{15}N]2-amino-4,6-dichloropyrimidine **18** and 18% of the undesired [4-^{15}N]4-amino-2,6-dichloropyrimidine **19**. Analysis of the material left in the thimble indicated less than 3% of product **18** remained.

[2-^{15}N]2-Amino-4,6-dimethoxypyrimidine, **20** *and [4-^{15}N]4-Amino-2,6-dimethoxypyrimidine,* **21**. To the 82/18 mixture of products **18** and **19** (5.65 g, 29.0 mmol) was added 65 ml of anhydrous MeOH and 25% NaOMe (34.4 ml, 168 mmol). The reaction was refluxed for 7.5 h, cooled to RT and AcOH (7 ml) was added. The mixture was diluted with water (150 ml), Na_2CO_3 was added until the pH = 9 and was extracted with ether (100 ml × 3). The combined ether extracts were dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation to give 5.15 g of a white powder. The product was purified by silica gel flash column chromatography with 40% EtOAc/60% hexane to give 3.97 g (88% yield) of white crystalline solid. ^{1}H-NMR (300 MHz, DMSO-D_6) δ 6.56 (d, J = 89.0 Hz, 2 H, 2-$^{15}NH_2$), 5.36 (s, 1 H, 5-H), 3.77 (s, 6 H, OCH_3). None of the 4-amino isomer was present by ^{1}H-NMR or by TLC analysis on silica using 40% EtOAc/60% hexane. The R_f of the 2-amino isomer **21** was 0.54 whereas the 4-amino isomer **20** had an R_f of 0.26.

N-[4,6-Dimethoxy-2-pyrimidinyl[^{15}N-amino]carbonyl]-2-(ethylsulfonyl)-imidazo[1,2a]pyridine-3-sulfonamide, **22**. To a flame-dried flask containing 2-ethylsulfonylimidazo[1,2*a*]pyridine-3-sulfonamide **15** (8.99 g, 31.0 mmol) was added 50 ml anhydrous MeCN and Et_3N (8.64 ml, 62.0 mmol). The solution was cooled to −5°C in a saltwater ice bath. To the reaction was added phenyl chloroformate (3.97 ml, 31.6 mmol) in 5.0 ml MeCN dropwise keeping the temperature below 10°C. The solution was warmed to RT and stirred for 1 h. [2-^{15}N]2-Amino-4,6-dimethoxypyrimidine **21** (3.58 g, 31.0 mmol) was added in one portion and the mixture was warmed to 55°C. CH_3SO_3H (2.00 ml,

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31.0 mmol) in 3 ml MeCN was added dropwise keeping the temperature between 50 and 55°C. The reaction mixture was stirred at 50–55°C for 1.2 h and then cooled in an ice water bath for 2 h. The precipitate was filtered, washed with cold water (5 ml) and cold MeCN (5 ml) and then dried under vacuum to give 9.82 g (67% yield, overall yield = 28% from 2,4,6-trichloropyrimidine) of the desired product **22** as a white powder. The isotopic enrichment was determined to be 97.8% ^{15}N and the chemical purity was determined to be 100% by HPLC. The melting point of the ^{15}N material was 198°C (reference MP = 197–199°C). MS analysis using LC-FAB (–) ion agreed with that expected with a molecular ion at $m/z = 470$. ^{1}H-NMR (300 MHz, DMSO-D_6) δ 13.15 (s, 1 H, ^{14}N-H); 10.77 (d, $J = 90$ Hz, 1 H, ^{15}N-H); 9.19 (d, $J = 7.1$ Hz, 1 H, Ar-H); 7.99 (d, $J = 9.1$ Hz, 1 H, Ar-H); 7.80 (t, $J = 8.0$ Hz, 1 H, Ar-H); 7.49 (t, $J = 7.1$ Hz, 1 H, Ar-H); 6.00 (s, 1 H, Ar-H); 3.94 (s, 6 H, OCH_3); 3.59 (q, $J = 7.4$ Hz, 2 H, CH_2); 1.16 (t, $J = 7.4$ Hz, 3 H, CH_3).

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