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PREPARATION OF CARBON-14 LABELED N-(2,6-DICHLORO-3-METHYLPHENYL)-5,7-DIMETHOXY[1,2,4]TRIAZOLO[1,5-A]PYRIMIDINE-2-SULFONAMIDE

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SUMMARY

A new 6-step process was developed for the synthesis of radiolabeled metosulam, a broadleaf post emergent herbicide being commercialized by DowElanco for use in small grains. Each step of the process can be accomplished in >80% yield thereby making the process a convenient and efficient route for the preparation of both radiolabeled and unlabeled samples of metosulam. A significant improvement was made in the coupling of the silylaniline with the sulfonyl chloride over the previously reported procedure which represents a key step in the process.

Key Words: metosulam, N-(2,6-dichloro-3-methylphenyl-Ph-UL-^{14}C)-5,7--dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide, N-(2,6-dichloro-3-methylphenyl)-5,7-dimethoxy[l,2,4]triazolo[l,5a]pyrimidine-2-sulfonamide-2-^{14}C, 2-benzylthio-5,7-dihydroxy[1,2,4]triazolo[1,5-a]pyrimidine2-^{14}C, 2-benzylthio-5,7-dichloro[1,2,4]triazolo[1,5-a]pyrimidine2-^{14}C, 2-chlorosulfonyl-5,7-dichloro [1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C

INTRODUCTION

N-(2,6-Dichloro-3-methylphenyl)-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide is currently being commercialized as a broad spectrum herbicide for use in small grains. It has been assigned the common name of metosulam. Samples with the carbon-14 label in the triazole ring and the phenyl ring respectively were required to conduct the studies essential for the registration of this product. The synthesis of metosulam has previously been reported (1-3). A new process was developed for the synthesis of radiolabeled metosulam.

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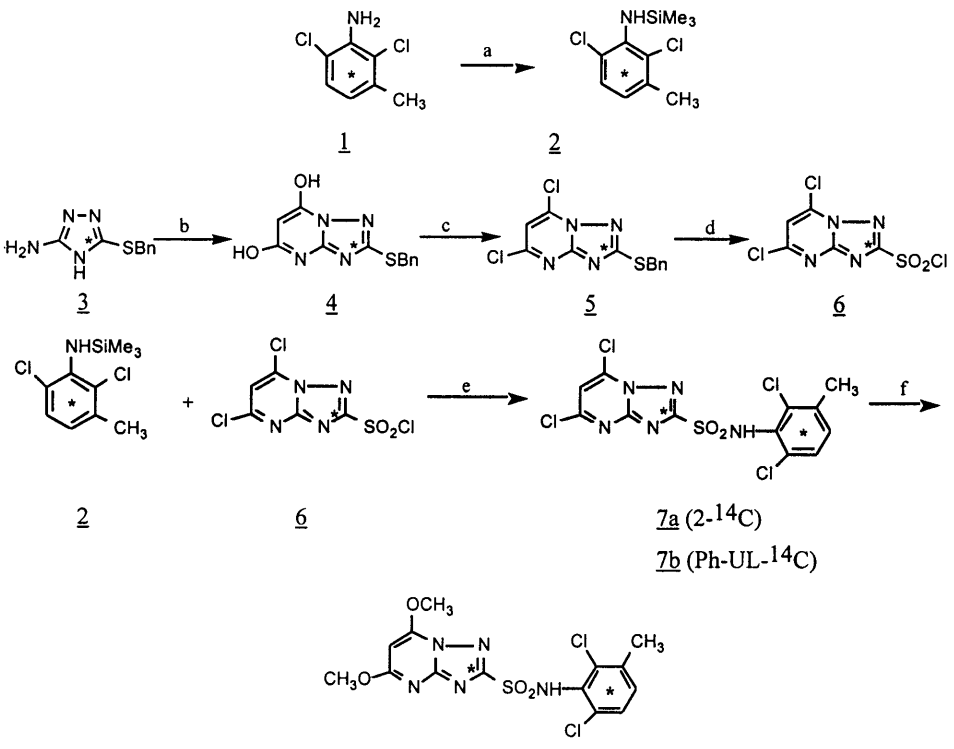
RESULTS AND DISCUSSION

Metosulam was independently labeled in the 2-position of the heterocycle and in the phenyl ring as described below.

Scheme I



Metosulam

* Metosulam independently labeled in each position.

(a) Et_2O, Me_3SiI, 24°C (b) dimethyl malonate, n-propanol, NaOPr, reflux (c) $POCl_3$, 95°C (d) aq. HCl, CH_2Cl_2, Cl_2, 5°C (e) CH_3CN, DMSO, -10°C (f) NaOMe, MeOH, 24°C

Conversion of aniline 1 to silylaniline 2 occurs in nearly quantitative yield. Conversion of triazole 3 to triazolopyrimidine 4 is best accomplished in n-propanol using sodium n-propoxide as the base. Higher yields (100%) of 4 are achieved than when butanol/sodium butoxide is used (73%) and the reaction time is much shorter (5 hr verses 65 hr) than when ethanol/sodium ethoxide is used. An alternate route to 4 involves the reaction of 3 with methyl malonyl chloride in refluxing acetonitrile using potassium carbonate as the base. The reaction is complete within 1.5 hours and affords an 82% yield of 4.

Reaction of 4 with excess phosphoryl chloride at 95°C affords a quantitative yield of dichloropyrimidine 5. The 95°C temperature is important. Lower yields of 5 will result if the reaction is conducted at reflux. The chloro-oxidation of 5 to 6 was accomplished in a dilute aqueous hydrochloric acid/methylene chloride mixture using chlorine as the oxidant. Although a quantitative yield of crude product was isolated, the actual yield of 6 was not determined in the tracer synthesis. However, in the pilot run (unlabeled reactants), an 85% yield of product was obtained based upon its purity.

2,6-Dichloro-3-methylaniline 1 affords very low yields of sulfonamide 7 when coupled with sulfonyl chloride 6 which was the major reason for the development of the reported processes (1-3). However, N-trimethylsilylanilines are much better nucleophiles with respect to the sulfonyl chlorides (4, 5) than are the corresponding anilines. The reactions were typically conducted using 2 equivalents of the trimethylsilylaniline and 1 equivalent of pyridine or 0.1 equivalent of dimethyl sulfoxide. In the above case, pyridine affords very low yields of sulfonamide 7 whereas the use of dimethyl sulfoxide afforded a **ca**. 55% overall yield of 7 from sulfide 5 in the pilot run (unlabeled reactants). Unfortunately, when the process was applied to 2-chlorosulfonyl-5,7-dichloro[1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C (6), only 30-41% overall yields of radiolabeled 7a were achieved. The low yields are a result of the fact that sulfonamide 7 is unstable in dimethyl sulfoxide and gradually degrades over the 7-8 hour reaction period at 0°C. Attempts to replace dimethyl sulfoxide with titanium tetrachloride as the catalyst led to very low yields of product.

Since metosulam only degrades slowly in dimethyl sulfoxide (**ca**. 10%/hour at room temperature), methods were sought to enhance the rate of reaction. This was accomplished by using 1 equivalent of dimethyl sulfoxide at -10°C. The reaction was complete within 45 minutes and afforded an 86% yield of unlabeled 7 in the pilot run. The modified process was applied to N-trimethylsilylaniline-UL-^{14}C. Based upon recovered 2,6-dichloro-3-methylaniline-UL-^{14}C, a 94% yield of radiolabeled 7 was isolated. The modified process has since been applied to several other triazolopyrimidines with good to excellent results in each case.

Reaction of unlabeled 7, isolated in an 86% yield *via* the modified process, with sodium methoxide afforded a 90% yield of unlabeled metosulam. When applied to the tracer syntheses, a 74% yield of

metosulam-2-^{14}C and a 70% yield of metosulam-Ph-UL-^{14}C were isolated. Both tracers were 99+% radiochemically pure *via* TLC and reverse phase HPLC analyses.

EXPERIMENTAL

All TLC analyses were conducted on either EM Laboratories 5 x 20 cm Kieselgel silica gel 60 F254 plates or Whatman 5 x 20 cm KC18F plates. The plates containing radioactivity were radioscanned using a Radiomatics RSTLC radioscanner. The data is listed as follows: plate used, solvent system, R_f, % radiochemical purity. The reverse phase HPLC analyses were conducted in a system consisting of a Water's 600E system controller, a Water's U6K injector, and a Water's Novapak C18 column (Water's 8 x 10 RCM) connected in series with a Water's 990 Photodiode Array UV detector and a Beckman 171 Radioisotope detector under the following conditions: (A) 100% H_2O to 100% CH_3CN, linear gradient at 2 mL/min for 25 min, 100% CH_3CN at 2 mL/min for 5 min or (B) 100% H_2O to 100% CH_3CN linear gradient at 1 mL/min over 50 min, 100% CH_3CN at 2 mL/min for 10 min. Both solvents contained 1% HOAc. The GLC analyses were obtained using a Hewlett Packard 5830A instrument equipped with a 14 m x 0.53 mm x 1.5 μ DB-1 column, Temp 1=50°C, Time 1=2 min, Rate=20°C/min, Temp 2=250°C, Time 2=10 min, N_2 Flow=17 mL/min, Inj Temp=200°C, FID Temp=300°C. The results are given as area%. No internal standards were used. Direct probe mass spectral analyses were conducted in a Finnigan 4615 instrument: EI mode, 70 eV, 1100 volts.

2,6-Dichloro-3-methyl-N-trimethylsilylaniline-Ph-UL-^{14}C (2)

2,6-Dichloro-3-methylaniline-Ph-UL-^{14}C was prepared by the previously described procedure (6). A 2.54 mmole sample of radiolabeled 1 (61 mCi at an approximate specific activity of 24 mCi/mmole) was dissolved in a solution consisting of 10 mL of Et_2O and 7 mL of n-pentane and 450 μL (3.23 mmole) of triethylamine added. The solution was stirred and 440 μL (3.09 mmole) of iodotrimethylsilane added causing immediate precipitation. The mixture was stirred for 23 hr, filtered, and the precipitate rinsed with Et_2O. The solvent was removed from the filtrate *in vacuo* . The residue was dissolved in 2 mL of Et_2O and filtered through $MgSO_4$ into a tared flask. The original flask was rinsed with several portions of Et_2O and each filtered into the tared flask. The solvent was removed *in vacuo* to afford 597.3 mg (2.41 mmole, 94.9% yield) of 2-Ph-UL-^{14}C as a light red oil, GLC (condition A) 6.56 min (97.1%).

Unlabeled 2 was prepared in a similar fashion except that n-pentane was not used as a co-solvent. Similar product yields are achieved.

2-Benzylthio-5,7-dihydroxy[1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C (4)

3-Amino-5-benzylthio[1,2,4]triazole-5-^{14}C 3 (Sigma Radiochemicals, Lot# 078F9234, Inventory #683, 100 mCi, 25.8 mCi/mmole, 3.876 mmole) was transferred from the vial to a 100-mL round bottom flask using CH_2Cl_2. The vial was rinsed with CH_3CN (2 x 1 mL, 3 x 0.5 mL) and CH_2Cl_2 (5 x 1 mL). The solvent was removed *in vacuo* and the solid dried at 24°C/25 mm for 1 hr. A 25-mL round bottom flask containing a side arm and equipped with a stir bar was dried under N_2 using a heat gun. Anhydrous n-propanol (10 mL) was added followed by 364.9 mg (15.86 mmole) of sodium. The stirred mixture was heated to reflux under a N_2 atmosphere causing complete reaction of the Na and affording a clear yellow solution within 0.5 hr. The solution was cooled in an ice bath and transferred to the 100-mL reaction flask containing the tracer using a 10-mL syringe. The 25-mL flask was rinsed with 2 x 1 mL of n-PrOH. The mixture in the reaction flask was stirred for 5 min and 2.0 mL (17.5 mmole) of dimethyl malonate added. The solution was heated at 104-108°C under a N_2 atmosphere for 5 hr. The mixture was cooled and allowed to stand overnight. The solvent was removed *in vacuo* and the residual solid dissolved in 15 mL of H_2O and extracted with 3 x 5 mL of EtOAc. The EtOAc extracts were washed with 3 x 1 mL of H_2O, which were added to the aqueous layer. The aqueous layer was freed from residual EtOAc using a stream of N_2. Copious precipitation resulted at this time and the solids would not dissolve *via* addition of 5 mL of H_2O. The mixture was acidified with 2.0 mL of conc. HCl and filtered. The precipitate was washed with 3 x 5 mL of H_2O. The precipitate was slurried in 5 x 5 mL of MeOH, which only partially dissolved the solids. The solvent was collected in a tared 100-mL bell shaped flask. The solids remaining in the reaction flask and filter were removed with 4 x 20 mL of refluxing MeOH and were collected in the tared flask. The solvent was removed *in vacuo* and the residue dried at 55°C/2 mm for 1 hr to afford 1.2924 g (4.712 mmole, ca. 100% yield) of 2-benzylthio-5,7-dihydroxy[1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C (4) as a white solid containing a small amount of yellow impurity. HPLC (Condition A) 11.5 min (97.91% radiochemically pure).

2-Benzylthio-5,7-dichloro[1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C (5)

The radiolabeled 4 was treated with 13 mL of $POCl_3$ and the mixture heated at 92-95°C for 23 hr.

The mixture was cooled, concentrated *in vacuo*, and the residual oil treated with a few grams of ice, 10 mL of H_2O, and 5 mL of CH_2C1_2. The phases were mixed for 0. 5 hr and the CH_2C1_2 phase transferred to a column containing 10 g of Merck silica gel G60 (60 A) packed in CH_2C1_2. The aqueous layer was extracted with 4 x 2 mL of CH_2C1_2 and each added to the column. The column was eluted with 1% EtOAc in CH_2Cl_2. Product was observed as a yellow band after **ca**. 25 mL of solvent had eluted and was isolated in 55 mL of solution. The solvent was removed *in vacuo* and the residue dried at 55°C/2 mm for 1 hr affording 1.2456 g (3.720 mmole at 92.9% purity, 96.1% yield from 3) of pyrimidine 5 as a yellow oil which solidified upon standing. HPLC (UV, 254 nm, Condition A) 21.56 min (92.9%).

2-Chlorosulfonyl-5,7-dichloro[1,2,4]triazolo[1,5-a]pyrimidine-2-^{14}C (6)

One mL of 1N HC1 was added to 6 mL of H_2O and the resultant solution added to pyrimidine 5 while cooling in an ice bath. The flask was equipped with a stir bar and a 3-way stopcock, to which was attached a Cl_2 filled (15" diameter) double balloon (the first inserted into the second). The flask was evacuated and filled with $C1_2$ three times. The flask contained a side arm which had been sealed with a septum. A 15-mL aliquot of CH_2C1_2 was added through the septum and the mixture stirred at 5°C for 1.25 hr. The mixture was purged with N_2 to remove the excess $C1_2$, treated with 2.0 g of $NaHSO_3$, and the CH_2C1_2 phase filtered through $Na_2SO_4/MgSO_4$ into a tared 100-mL round bottom flask. The aqueous phase was extracted with 4 x 2 mL of CH_2C1_2 and each filtered into the flask. The solution was analyzed *via* reverse phase HPLC (Condition A): 15.64 min, 81.6%. The solvent was removed from the filtrate *in vacuo*. The residual oil was triturated with 2 x 5 mL of n-pentane. The oil crystallized during the second trituration. After each trituration, the solvent was removed *via* a filter stick and filtered through a pipet containing a glass wool plug to collect the trace solids on the filter stick. The solid was washed with 2 x 2 mL of n-pentane. The solid remaining on the filter stick and in the filter were dissolved in CH_2C1_2 and added to the precipitate in the flask. The solvent was removed under a stream of N_2 and the residue dried at 24°C/25 mm for 0.5 hr to afford 1.1948 g of sulfonyl chloride 6 as a light yellow solid.

N-(2,6-Dichloro-3-methylphenyl)-5,7-dichloro[l,2,4]triazolo(l,5-a)pyrimidine-2-sulfonamide-2-^{14}C (7a)

To the 100-mL flask containing the radiolabeled sulfonyl chloride 6 was added 5 mL (1.12 g/mL,

22.6 mmole) of 2,6-dichloro-3-methyl-N-trimethylsilylaniline and 5 mL of CH_3CN, which had been dried *via* distillation from P_2O_5. The solution was stirred and DMSO added as follows: 0.0 hr (25 μL), 1.33 hr (25 μL), 2.5 hr (10 μL), 3.67 hr (10 μL), 4.33 hr (10 μL), 6.33 hr (10 μL). The reaction was followed by TLC (1 x 4" Analtech silica gel GF plate, 3:6.5:0. 5 EtOAc:hexane:HOAc, R_f 6=0.51, R_f 7a=0.35, R_f silylaniline=0.71) and was nearly complete after 7 hr. After 8.33 hr, the CH_3CN was removed under a stream of N_2. The residual oil was cooled in an ice bath and treated with 10 mL of n-pentane and a solution consisting of 2 mL of conc. HCl in 10 mL of H_2O. The mixture was stirred, filtered, and the precipitate washed with 3 x 4 mL of 1:1 H_2O:Et_2O (v/v). The solid was slurried in acetone and transferred to the tared 100-mL flask used for the reaction. The filter was rinsed with refluxing acetone. The solvent was removed *in vacuo* and the residue dried at 55°C/2.5 mm for 1 hr to afford 735.5 mg of sulfonamide 7a as a white solid. HPLC (Condition A, 280 nm) 17.49 min (65.0% pure, 30.1% overall yield from sulfide 5).

N-(2,6-Dichloro-3-methylphenyl)-5,7-dimethoxy[l,2,4]triazolo[l,5-a]pyrimidine -2-sulfonamide-2-^{14}C (metosulam-2-^{14}C)

A NaOMe solution was prepared by reacting 146.4 mg (6.365 mmole) of sodium in 5 mL of MeOH. The radiolabeled 7a was cooled in an ice bath and the NaOMe solution added. The flask containing the NaOMe solution was rinsed with 2 x 1 mL of MeOH. The ice bath was removed and the mixture stirred for 1 hr. The mixture was acidified with 0.6 mL (10.5 mmole) of HOAc and concentrated to **ca**. 5 mL under a stream of N_2. A 2-mL aliquot of 1N HCl was added to the stirred mixture. The mixture was filtered and the precipitate extracted with 1 x 2 mL of 1N HCl, 2 x 5 mL of H_2O, and 2 x 1 mL of MeOH while cooling in an ice bath. The precipitate was dissolved in 55 mL of refluxing acetone and filtered into a tared 100-mL round bottom flask. The reaction flask and filter were rinsed with 5 x 2 mL of refluxing acetone. The final filtrate was heated to reflux to re-dissolve the precipitate and a 0.2 μL aliquot analyzed *via* reverse phase HPLC (Condition A) affording product of 92.5% radiochemical purity. The solvent was removed *in vacuo* and the residue dried at 50°C/2.5 mm to afford 518.3 mg of metosulam-2-^{14}C as a tan solid. The tracer was dissolved in 50 mL of refluxing acetone and the refluxing solution concentrated to **ca**. 25 mL. MeOH, 25 mL, was added at reflux and the solution again concentrated to 25 mL causing precipitation. An additional 25 mL of MeOH was added at reflux and the refluxing mixture concentrated to 25 mL. The mixture was cooled to room temperature and finally cooled at -22°C (freezer) overnight. The mother liquor

was removed *via* filter stick and filtered through a coarse fritted glass filter. The precipitate was rinsed with 2 x 1 mL of cold MeOH (5°C). The filter stick and filter were rinsed with refluxing acetone and the rinses collected with the precipitate. The acetone was removed under a stream of N_2 and the residue dried *in vacuo* at 55-60°C/2.0 mm to a constant weight affording 392.3 mg (O.9378 mmole, 83.8% yield, 24.2% overall yield) of metosulam-2-^{14}C as a white solid possessing a specific activity of 27.0 mCi/mmole (25.3 mCi). TLC (SiO_2, 20:20:10 EtOAc:hexane:HOAc) R_f 0.52, 100%; (SiO_2, 35:15 toluene:HOAc) R_f 0.29, 100%; (SiO_2, 35:10:5 EtOAc:toluene:HOAc) R_f 0.25, 100%; (KC18F, 35:13:2 MeOH:H_2O:HOAc) R_f 0.63, 100%; HPLC (Condition B) 31.82 min, 99.8%; MS 417, 419 & 421 (M^+), 382, 384 & 386 (M^+-Cl). The tracer had been compared with a standard sample of metosulam during the above analyses and, except for the mass spectral data which showed the effects of the carbon-14 label, afforded identical results.

N-(2,6-Dichloro-3-methylphenyl-Ph-UL-^{14}C)-5,7-dichloro[1,2,4]triazolo [1,5-a]pyrimidine-2-sulfonamide (7b)

The flask containing the 2.4 mmole of silylaniline 2 was equipped with a stir bar and 342.3 mg (1.191 mmole) of unlabeled sulfonyl chloride 6 (prepared as described above) and 0.5 mL of CH_3CN added. The stirred solution was cooled to -14°C in an ice-acetone bath and 86 µL (1.21 mmole) of DMSO added. The solution was stirred at -10° to -14°C for 45 min. The cold solution was treated with 100 µL (5.55 mmole) of H_2O, and the CH_3CN removed under a stream of N_2. The residual solid was extracted with 1 x 5 mL and 5 x 2 mL of n-pentane to remove the unreacted aniline 1 and each extract added to a column packed dry with 10 g of Merck silica gel G60 (230-400 mesh). The solid was extracted with 3 x 1 mL of Et_2O and the extracts analyzed ***via*** TLC (1 x 4" SiO plate, 3:6.5:0.5 EtOAc:n-hexane:HOAc) to contain aniline 1. The solid was extracted with 3 x (1 mL H_2O + 1 mL Et_2O). The Et_2O was separated from the H_2O layer and combined in a 50-mL flask with the previous Et_2O extracts. The H_2O layer was extracted with 2 x 1 mL of Et_2O and each added to the flask. The precipitate was dried *in vacuo* at 60-65°C/3 mm to afford 393.2 mg (0.921 mmole, 77.3% yield based on sulfonyl chloride 6) of sulfonamide 7b as a light yellow solid.

The solvent was removed from the Et_2O extracts *in vacuo* at 24 °C/40 mm. The residue was extracted with 6 x 1 mL of n-pentane and each added to the above silica gel column. The column

was eluted with n-pentane. Radioactivity was observed after 30 mL of solvent had eluted and was isolated in 70 mL of solution. The n-pentane was removed *in vacuo* at 24 °C/40 mm and the residue dried at 24 °C/20 mm to afford 267.9 mg (1.486 mmole at 97.7% purity by GLC) of 2,6-dichloro-3-methylaniline-Ph-UL-^{14}C as a white solid. The recovered 1 was converted to silylaniline 2 . Silylaniline 2 (1.44 mmole) was treated with 208.7 mg (0.726 mmole) of unlabeled sulfonyl chloride 6 and 0.5 mL of CH_3CN and cooled to -14 °C. DMSO, 51 μL (0.72 mmole), was added and the solution stirred at -9° to -14°C for 1 hr. The solution was concentrated at -9°C under a stream of N_2 and the residue extracted with 3 x (1 mL H_2O + 1 mL Et_2O) and 1 x 1 mL of Et_2O. The remaining solid was transferred to the tared flask containing the previously isolated sulfonamide 7 initially by slurring it in acetone and finally by dissolving the last traces in refluxing acetone. The solvent was removed *in vacuo* and the residue dried at 60°C/3.5 mm to afford 291.3 mg (0.6820 mmole, 93.9% yield) for the second reaction and 684.5 mg total of sulfonamide (7) as a light yellow solid, 96.1% pure by HPLC (1.54 mmole). The unreacted aniline was isolated as previously described to afford 123.3 mg (0.700 mmole, 29.2% recovery) of 1 as a white solid (100% pure *via* GLC).

Metosulam-Ph-UL-^{14}C

A methanolic NaOMe solution was prepared by reacting 332.1 mg of Na in **ca**. 7 mL of MeOH in a 10-mL volumetric flask and filling the flask to volume with MeOH. A 0.5-mL aliquot of the solution was diluted with H_2O and titrated to the phenolphthalein endpoint with 1.0 N HCl affording a 1.36 N NaOMe solution. The flask containing sulfonamide 7 was equipped with a stir bar, placed in an ice bath, and 4.71 mL of the NaOMe solution added. The ice bath was removed and the mixture stirred for 1 hr. The mixture was again cooled in the ice bath and acidified initially with 0.41 mL of HOAc (7.16 mmole) and subsequently with 0.6 mL of conc. HCl (ca. 37.4%, 1.194 g/mL, 7.34 mmole). The mixture was filtered and the precipitate washed with 2 x 1 mL of cold MeOH and 5 x 1 mL of H_2O. The precipitate was dissolved in 75 mL of refluxing acetone and filtered through Celite into a tared 250-mL round bottom flask. The reaction flask and filter were rinsed with refluxing acetone. The filtrate was concentrated to **ca**. 25 mL at reflux under a stream of N_2 and diluted with 25 mL of MeOH. The solution was concentrated to 25 mL at reflux, an additional 25 mL of MeOH added, and the solution again concentrated to 25 mL causing copious precipitation. The mixture was initially cooled in an ice bath and subsequently in a -22°C freezer

overnight. The mixture was filtered and the precipitate washed with 2 x 1 mL of cold (5°C) MeOH. The filtrate was discarded. The precipitate was dried at 60°C/3.5 mm to afford 462.2 mg (1.105 mmole) of metosulam-Ph-UL^{14}C as a white solid. The product was 97.6% radiochemically pure by reverse phase HPLC with one major impurity believed to be the mono-methoxy adduct. The product was suspended in 5 mL of MeOH, cooled in an ice bath, and 1.6 mL (2.30 mmole) of a 1.44 N NaOMe solution added. The solution was stirred at 5°C for 0.5 hr causing slight precipitation. The mixture was treated with 158 µL of HOAc (2.76 mmole) and 2.5 mL of 1.0 N HC1. The mixture was stirred, filtered, and the precipitate washed with 3 x 1 mL of H_2O and 2 x 1 mL of MeOH. The precipitate was dried i*n vacuo* at 60°-65°C/3.5 mm for 1.5 hr to afford 453.3 mg (1.084 mmole, 70.4% yield) of product as a white solid. Subsequent analyses afforded 24.98 mCi of metosulam-Ph-UL-^{14}C with a specific activity of 23.0 mCi/mmole. TLC (SiO_2, 25:15:10 EtOAc:hexane:HOAc) R_f 0.56, 99.9%; (SiO_2, 30:20 toluene:HOAc) R_f 0.55, 100%; (SiO_2, C_6H_6:HOAc) R_f 0.62, 100%; (KC18F, 35:13:2 MeOH:H_2O:HOAc) R_f 0.59, 100%; HPLC (Condition B) 32.22 min, 99.99%; MS 417, 419 & 421 (M^+), 382, 384 & 386 (M^+-Cl). The tracer had been compared with a standard sample of metosulam during the above analyses and, except for the mass spectral data which showed the effects of the carbon-14 label, afforded identical results.

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