SYNTHESIS OF CARBON-14 LABELLED INDOLIC $5HT_1$ RECEPTOR AGONISTS

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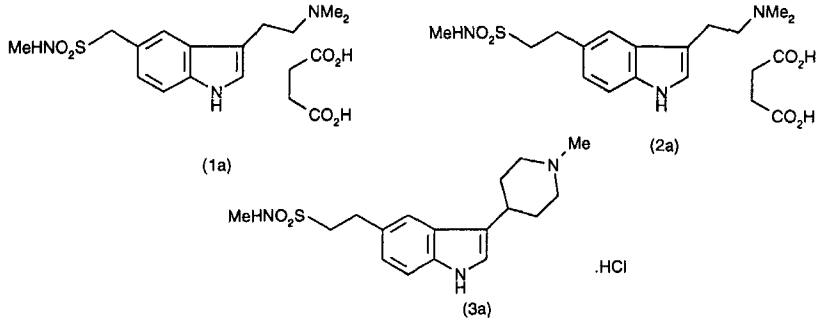
Summary

Syntheses of carbon-14 labelled versions of indolic $5HT_1$ agonists sumatriptan (GR43175) (1a), GR40370 (2a) and naratriptan (GR85548) (3a) are described. Introduction of the label *via* cyanation of ketoformanilides, formed by oxidative cleavage of an indole ring, ensured incorporation of carbon-14 at the metabolically stable C-2 position of the indole.

Keywords: carbon-14, indole, 5HT $_1$ receptor agonist.

Introduction

Sumatriptan (1a) is a selective $5HT_1$ agonist, which has proved to be an effective new treatment for migraine (1). As part of the development programme in this therapeutic area, carbon-14 labelled versions of sumatriptan (1a) (GR43175) and analogues GR40370 (2a) and naratriptan (3a) (GR85548) (2) were required for pharmacokinetic studies and metabolite profiling work.



It was established (3) that a carbon-14 label sited in the methanesulphonamido group of sumatriptan was metabolically unstable, being lost as carbon dioxide. As the dimethylaminoethyl chain in sumatriptan was also judged to be vulnerable to metabolism, a method of incorporating a label into the indole nucleus was sought.

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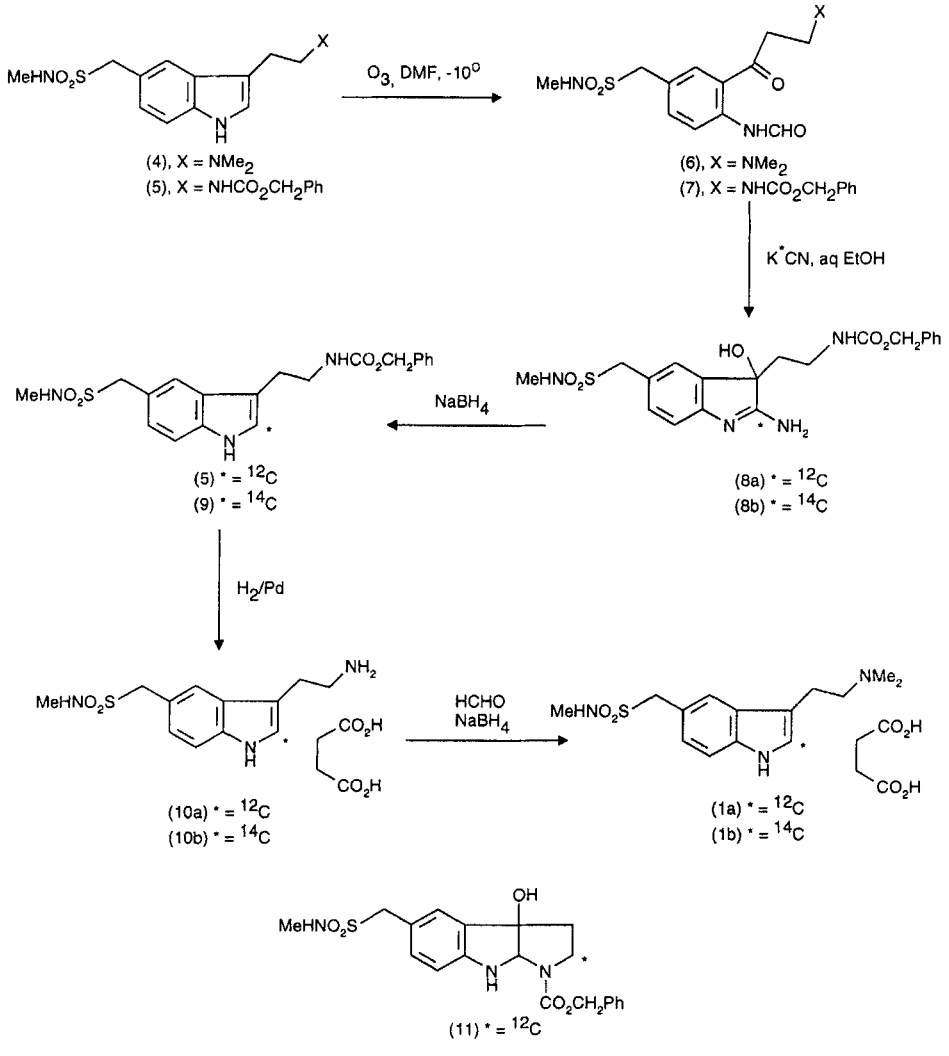
Scheme 1



Results and Discussion

[^{14}C]-Labelled GR43175

Utilising procedures described in the peptide literature (4), it was envisaged that the key intermediates in the syntheses of labelled indoles would be the corresponding ketoformanilides, derived from the parent drug by oxidative cleavage of the indole ring. However, treatment of sumatriptan free base (4) with either ozone or sodium periodate gave intractable mixtures, in which none of the required product (6) was detected (Scheme 1). However, it was found possible to cleave the related CBZ derivative (5), a potential precursor of sumatriptan, to ketone (7), using ozone (33% yield). When the

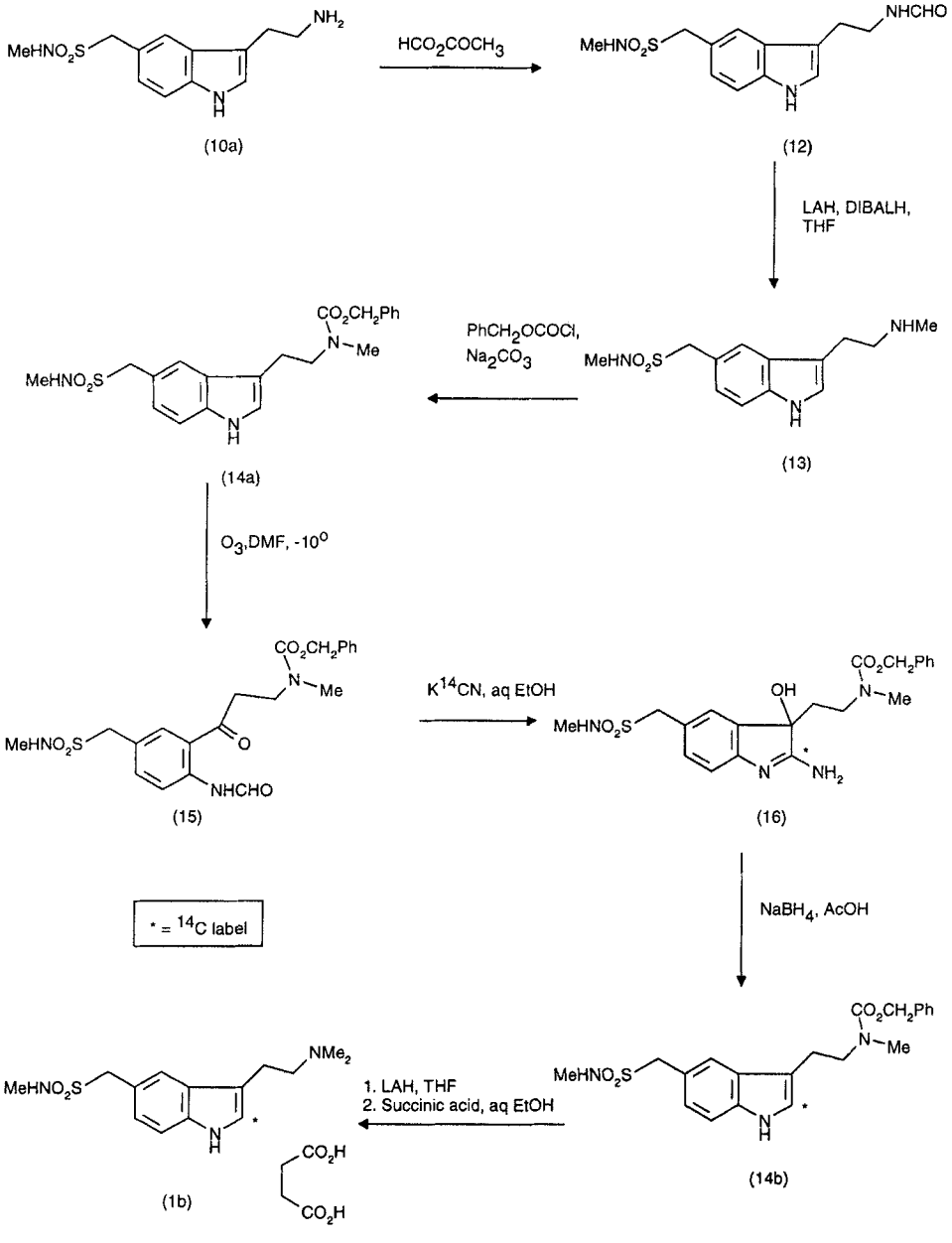
amidine (8a) was formed (60% yield), and subsequently reduced in aqueous ethanol, the product was found to contain a mixture of the required indole (5) and the tricyclic adduct (11) (ca.1:1). This ratio could be improved to *ca.* 4:1 by conducting the reduction of (8a) in acetic acid, giving the indole (5) in 70% isolated yield. Hydrogenolysis then provided the primary amine (10a) (60%), which was reductively aminated with formaldehyde to give sumatriptan, isolated as its succinate salt (1a). The radiosynthesis from potassium [^{14}C]cyanide proceeded in a similar manner, giving [^{14}C]sumatriptan (1b) in 16% overall radiochemical yield. The radiochemical yield was improved to 26% by a combination of recycling unreacted primary amine (10b) and 'sweeping' the final succinate salt liquors with unlabelled material to obtain [^{14}C]sumatriptan of lower specific activity.

A significantly better overall yield of [^{14}C]sumatriptan was obtained using an alternative route, which avoided the problems of tricycle formation by performing the ring closure reaction on the CBZ derivative of a secondary, rather than a primary amine. This approach also avoided the inefficient reductive amination reaction. Thus, the primary amine (10a) (Scheme 2), an intermediate in the synthesis of unlabelled sumatriptan succinate, was converted into the formamide (12) on treatment with formic acetic anhydride. Attempted reduction of (12) with lithium aluminium hydride (LAH) gave insoluble complexes, which hindered further reaction. This problem was alleviated by addition of diisobutyl aluminium hydride before the LAH, presumably giving more soluble complexes. It was advantageous to allow the water soluble product (13) to react with benzyl chloroformate *in situ*, giving the crystalline carbamate (14a) in 76%overall yield from (12). Ozonolysis of (14a) in dimethylformamide at -10° proceeded smoothly to give the ketoformanilide (15) (66% after crystallisation), which was then allowed to react with potassium [^{14}C]cyanide (125mCi) in aqueous ethanol to form the amidine (16), which was reduced directly with sodium borohydride in acetic acid-tetrahydrofuran to give labelled indole (14b) in 80% radiochemical yield. Further reduction with LAH gave [^{14}C]sumatriptan free base which, after chromatographic purification, was isolated as the crystalline monosuccinate salt (1b) in 59% overall radiochemical yield from potassium [^{14}C]cyanide. The homologue GR40370 (2b) was prepared by the same methodology (Scheme 2, CH_2SO_2NHMe in place of SO_2NHMe) in 36% overall radiochemical yield.

[^{14}C]-Labelled naratriptan

Synthesis of a [^{14}C]-labelled version of the piperidinyl analogue GR85548 (naratriptan) (Scheme 3) was considerably more straightforward than the previous examples, since it was found possible to directly oxidise the parent compound to the intermediate ketoformanilide (17).

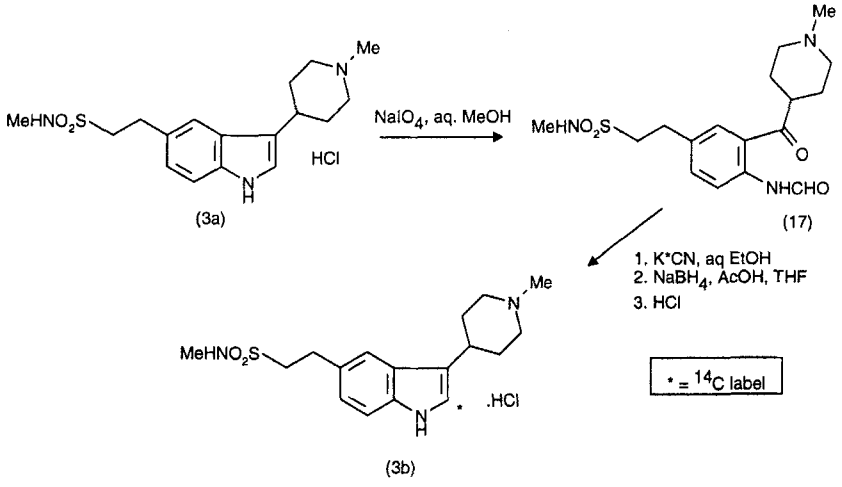
Scheme 2



Thus, treatment (5) of a solution of the hydrochloride salt (3a) in aqueous methanol with sodium periodate gave a smooth, though rather slow, conversion to the highly crystalline ketone (17). The reason for the difference in the behaviour of this compound and the analogues described above towards oxidation may be due to the increased chain length between the tertiary amine group and the newly formed ketone. In this case the product

(17) was a γ-aminoketone rather than a potentially unstable (*via* elimination) β-aminoketone which would be formed by ring cleavage of sumatriptan. The ring closure sequence proceeded in a similar manner to those described above to give the [^{14}C]indole (3b) in an overall yield of 67% from potassium [^{14}C]cyanide.

Scheme 3



Conclusion

Three indolic 5HT$_1$ receptor agonists, labelled with carbon-14 in the metabolically stable C-2 position have been prepared in good yield from potassium [^{14}C]cyanide. The method should have wider application in the synthesis of carbon labelled versions of other indolic compounds of biological interest.

Experimental

^{1}H NMR spectra were recorded on a Bruker AC250 spectrometer. Microanalyses were performed using a Carlo Erba 1108 elemental analyser. All column chromatography was carried out over Merck Kieselgel 60 (9385) silica gel. Radiochemical purities were determined either by TLC using a Berthold linear analyser, or by HPLC using a Canberra Packard Radiomatic Flo-one βeta detector with liquid scintillant detection.

[3-(2-Formylamino-5-methylsulphamoylmethylphenyl)-3-oxopropyl]carbamic acid benzyl ester (7)

Ozone enriched oxygen was passed into a solution of [2-(5-methylsulphamoylmethyl-1H-indol-3-yl)ethyl]carbamic acid benzyl ester (5) (1.85g, 5.86mmol) in dimethylformamide (47ml) for 6min, maintaining the temperature at -5° to -10°. Nitrogen was bubbled through the mixture for 5min, before it was poured into iced water (200ml), and extracted with ethyl acetate (150ml, 2x50ml).

The combined extracts were washed successively with water (40ml), 0.2%w/v sodium metabisulphite (45ml) and water (40ml), dried and evaporated. Purification by column chromatography over silica gel using diethyl ether-ethanol (10:1) as eluent gave the *title compound* as a white solid (699mg, 33%). m.p. 137-139.5°. δ_H (250MHz, DMSO-d_6) 11.15 (1H, br, C<u>H</u>O), 5.02 (2H, s, C<u>H</u>$_2$Ph), 4.43 (2H, s, C<u>H</u>$_2$SO$_2$), 2.42 (3H, d, C<u>H</u>$_3$NHO$_2$S). Found: C, 55.1; H, 5.3; N, 9.5; $C_{20}H_{23}N_3O_6S$ requires C, 55.4; H, 5.3; N, 9.7%.

[2-(5-Methylsulphamoylmethyl-1H-[2-^{14}C]-indol-3-yl)ethyl]carbamic acid benzyl ester (9)

Potassium [^{14}C]cyanide (190mg, 2.83mmol; 150mCi) was added to a stirred suspension of [3-(2-formylamino-5-methylsulphamoylmethylphenyl)-3-oxopropyl]carbamic acid benzyl ester (7) (1.227g, 2.83mmol) in ethanol-water (95:5) (20ml). The suspension was stirred at 20° for 5h to give a clear solution, which was partitioned between ethyl acetate (30ml) and water (60ml). The layers were separated and the aqueous layer extracted with ethyl acetate (3x15ml). The combined ethyl acetate extracts were washed with 10% brine solution (16ml), dried and evaporated under reduced pressure to give the amidine (8b) as a white foam (150mCi, 100%). TLC (ethyl acetate-isopropanol-water-ammonia, 25:15:2:2), radiochemical purity 95%. This foam was dissolved in glacial acetic acid (12ml), cooled to 12-14°, and sodium borohydride (406.3mg, 10.7mmol) added portionwise over 5min. After stirring for 20min, 2N hydrochloric acid (1.03ml) was added, the solution was diluted with water (8ml), and the product extracted into ethyl acetate (80ml, 2x40ml). The combined extracts were washed with 2N sodium carbonate solution (2x70ml, 2x40ml) and water (40ml), then dried and evaporated under reduced pressure to give a yellow oil. Purification by chromatography on a column of silica gel, using dichloromethane-ethanol (19:1) as eluent, yielded the *title compound* as a white foam (97.99mCi, 65%). TLC (dichloromethane-ethanol, 19:1), radiochemical purity 99%. A sample of unlabelled *title compound (5)* had been prepared similarly as a foam; δ_H (250MHz, CD_3OD) 5.10 (br s) and 4.94 (br s) (2H, C<u>H</u>$_2$Ph), 4.38 (br s) and 4.27 (br s) (2H, C<u>H</u>$_2$SO$_2$), 3.59 (2H, t, NC<u>H</u>$_2$CH$_2$), 2.98 (2H, m, NCH$_2$C<u>H</u>$_2$), 2.88 (3H, s, C<u>H</u>$_3$NHO$_2$S), 2.56 (br s) and 2.48 (br s) (3H, C<u>H</u>$_3$NCH$_2$).

C-[3-(2-Aminoethyl)-1H-[2-^{14}C]-indol-5-yl]-N-methylmethanesulphonamide succinate (10b)

[2-(5-Methylsulphamoylmethyl-1H-[2-^{14}C]-indol-3-yl)ethyl]carbamic acid benzyl ester (9) (1.85mmol, 97.99mCi) was dissolved in ethanol (35ml) and the solution hydrogenated over 10% palladium on charcoal (160mg) for 13.5h, further aliquots of catalyst being added after 4 and 6h. The catalyst was removed by filtration, and the filter cake washed with ethanol (8x20ml). Evaporation of the filtrate gave an oil, which was dissolved in hot ethanol (12ml), and treated with a hot solution of succinic acid (213mg, 1.90mmol) in ethanol (2ml). The mixture was heated under reflux for 5min then allowed to cool to room temperature. Ether (30ml) was added and the suspension was cooled at 0° for 30min. The solvent was removed and the oil washed with ether (2ml), then dried under high vacuum to give the *title compound* as a white foam (562mg, 78%; 76.9mCi). A further quantity (86mg, 12%, 11.8mCi) of (10b) was obtained by recycling the unreacted starting material remaining in the mother liquors. TLC (ethyl acetate-isopropanol-water-ammonia, 25:15:8:2), radiochemical purity 95%.

C-[3-(2-Dimethylaminoethyl)-1H-[2-^{14}C]-indol-5-yl]-N-methylmethanesulphonamide succinate (1b)

C-[3-(2-Aminoethyl)-1H-[2-^{14}C]-indol-5-yl]-N-methylmethanesulphonamide succinate (10b) (648mg, 1.674mmol, 88.8mCi) was partitioned between ethyl acetate (30ml) and 2N sodium carbonate solution (30ml). The phases were separated and the aqueous layer saturated with solid potassium carbonate and extracted with ethyl acetate (2x30ml). The combined ethyl acetate extracts were dried, filtered and evaporated under reduced pressure to give a light brown solid. The solid was dissolved in methanol (25ml) at 0°. Solutions of sodium borohydride (284mg, 7.5mmol) in water (1.7ml) and of formaldehyde (37% aqueous solution, 2.20ml, 27mmol) in methanol (1.93ml) were prepared. An aliquot (180µl) of the sodium borohydride solution was added to the solution of (10b) in methanol every 4min, followed each time by an aliquot (410µl) of the formaldehyde solution. When the additions were complete the reaction mixture was stirred at < 5° for lh. Sodium borohydride (30mg, 0.79mmol) and then 5N hydrochloric acid (3.2ml) were added and the mixture stirred for 5min then concentrated under reduced pressure to a volume of 10ml. Water (45ml) and 2N hydrochloric acid (25ml) were then added and the solution stirred for a further 10min. The solution was saturated with solid potassium carbonate and the product extracted into methyl isobutyl ketone (4x60ml). The methyl isobutyl ketone solution was decolourised with charcoal and evaporated under reduced pressure to a volume of 5ml, cooled to 0° and ether (10ml) was added. After storing at 0° for 30min, the resulting solid was recovered by filtration and crystallised from isopropanol-water to give sumatriptan free base (172mg, 35%, 30.6mCi). Treatment of this material with succinic acid (1eq) in hot ethanol (4ml) containing a little water gave, after cooling to 0° for 2h, the *title compound* (162mg, 67%, 24mCi) as a white solid with m.p. 166-7°. TLC (ethyl acetate-isopropanol-water-ammonia, 25:15:2:2), radiochemical purity 98%; δ_H (250MHz, D_2O) 4.58 (2H, br s, CH_2SO_2), 3.46 (2H, t, NCH_2CH_2), 3.23 (2H, m, NCH_2CH_2), 2.92 (6H, s, $N(CH_3)_2$), 2.74 (3H, s, CH_3NHO_2S), 2.52 (4H, s, succinate CH_2x2).

C-[3-(2-Formylaminoethyl)-1H-indol-5-yl]-N-methylmethanesulphonamide (12)

Acetic formic anhydride was prepared by dropwise addition of 98% formic acid (0.6ml, 16mmol) to acetic anhydride (1.22ml, 13mmol) at 5° and then heating at 60° for 1.5h. After cooling to 5° under nitrogen, tetrahydrofuran (3ml) was added followed by C-[3-(2-aminoethyl)-1H-indol-5-yl]-N-methylmethanesulphonamide (10a) (1.337g, 5mmol). The brown solution was stirred at 20° for 2.5h then most of the solvents/reagents were removed *in vacuo*, 8% sodium bicarbonate solution (50ml) was added and the mixture extracted with ethyl acetate (5x30ml). Evaporation of the combined, dried extracts gave the *title compound* (1.456g, 99%) as a pale brown foam; δ_H (250MHz, CD_3OD) 4.39 (2H,s, CH_2SO_2), 3.44 (2H, m, NCH_2CH_2), 2.85 (2H, m, NCH_2CH_2), 2.52 (3H, s, CH_3NHO_2S).

Methyl-[2-(5-methylsulphamoylmethyl-1H-indol-3-yl)ethyl]carbamic acid benzyl ester (14a)

Diisobutylaluminium hydride (1M in hexane; 43.4ml) was added dropwise to a solution of C-[3-(2-formylaminoethyl)-1H-indol-5-yl]-N-methylmethanesulphonamide (12) (6.41g, 21.7mmol) in dry tetrahydrofuran (150ml). Lithium aluminium hydride (825mg, 21.7mmol) was then cautiously added, and the mixture heated under reflux for 5h. More lithium aluminium hydride (466mg,

12.26mmol) was then added, and heating continued for a further 6h. The reaction mixture was quenched with isopropanol, then 2N sodium carbonate solution (75ml) and benzyl chloroformate (6.2ml, 43.4mmol) were added and the slurry allowed to stand at 20° overnight. The mixture was then poured into 2N hydrochloric acid (750ml) and extracted with ethyl acetate (2x250ml). Evaporation of the combined extracts gave a gum which was purified by chromatography over silica gel using diethyl ether - ethyl acetate (92:8) as eluent to give the *title compound* (6.89g, 76%) as a white solid with m.p. 120-121°. TLC (diethyl ether-ethyl acetate, 92:8) Rf 0.30; δ_H (250MHz,CD_3OD) 5.10 (br s)and 4.94 (br s) (2H, $C\underline{H}_2Ph$), 4.38 (br s) and 4.27 (br s) (2H, $C\underline{H}_2SO_2$), 3.59 (2H, t, $NC\underline{H}_2CH_2$), 2.98 (2H, m, $NCH_2C\underline{H}_2$), 2.88 (3H, s, $C\underline{H}_3NHO_2S$), 2.56 (br s) and 2.48 (br s) (3H, $C\underline{H}_3NCH_2$).

[3-(2-Formylamino-5-methylsulphamoylmethylphenyl)-3-oxopropyl]methylcarbamic acid benzyl ester (15)

Methyl-[2-(5-methylsulphamoylmethyl-1H-indol-3-yl)ethyl]carbamic acid benzyl ester (14a) (1.09g, 2.63mmol) was dissolved in dry dimethylformamide (25ml) and the mixture cooled to *ca.* -10°. Ozone enriched oxygen was bubbled through the solution for 5min. Nitrogen was bubbled through for 10min then the mixture was poured into aqueous sodium metabisulphite and extracted with ethyl acetate (3x50ml). The combined extracts were washed with water, 2% sodium metabisulphite solution and water then concentrated under reduced pressure to give a brown oil. This was crystallised from dichloromethane- diethyl ether to give the *title compound* (780mg, 66 %) as a buff solid. M.p. 123-125°. TLC (ethyl acetate), Rf 0.5; δ_H (250MHz, DMSO-d_6) 5.08 (2H, s, $C\underline{H}_2Ph$), 2.72 (3H, d, $C\underline{H}_3NHO_2S$), otherwise uninformative due to restricted rotation. Found: C,56.1; H,5.7; N,9.3; S,7.1. $C_{21}H_{25}N_3O_6S$ requires C,56.4; H,5.6; N,9,4; S,7.2%.

Methyl-[2-(5-methylsulphamoylmethyl-1H-[2-^{14}C]-indol-3-yl)ethyl] carbamic acid benzyl ester (14b)

A mixture of [3-(2-formylamino-5-methylsulphamoylmethylphenyl)-3-oxopropyl]methyl carbamic acid benzyl ester (15) (1.036gm, 2.32mmol) and potassium [^{14}C]cyanide (125.1mCi, 55.7mCi/mmol, 2.247mmol) in 95 % ethanol-water (20ml) was stirred at 20° for 4h. The resulting pale brown solution was added to dilute brine (150ml), and extracted with ethyl acetate (3x40ml). The combined extracts were dried and evaporated to give a sticky solid, which was dissolved in acetic acid (12ml) and tetrahydrofuran (6ml). The pale yellow solution was cooled to 5° and sodium borohydride (427mg, 11.237mmol) added over 15min at such a rate that the reaction temperature remained below 9°. After stirring for a further 25min at 5°, 2N hydrochloric acid (6ml) was added dropwise. The mixture then neutralised with aqueous sodium hydroxide, added to 2N sodium carbonate solution (100ml) and extracted with ethyl acetate (80ml, 2x40ml). The combined extracts were dried and evaporated and the residue purified by chromatography over silica, using diethyl ether-ethyl acetate (92:8 then 90:10) as eluent. The *title compound* was obtained as a pale brown gum (100.5mCi). TLC (dichloromethane-ethanol-ammonia, 15:6:1), radiochemical purity 98%. NMR data on an unlabelled sample prepared by the same method was identical to that described for (14a) above.

C-[3-(2-Dimethylaminoethyl)-1H-[2-^{14}C]-indol-5-yl]-N-methylmethanesulphonamide succinate (1b)

Methyl-[2-(5-methylsulphamoylmethyl-1H-[2-^{14}C]-indol-3-yl)ethyl] carbamic acid benzyl ester (14b) (100.5mCi) was dissolved in tetrahydrofuran (30ml), cooled to 5° under nitrogen and lithium aluminium hydride (206mg, 5.415mmol) added. The mixture was heated under reflux for 1.5h then cooled in ice, quenched with isopropanol (3ml) and added to a saturated aqueous solution of sodium potassium tartrate (120ml). The aqueous mixture was extracted with ethyl acetate (2x75ml) and the combined extracts dried and evaporated to give a solid. Trituration with ether yielded a fawn solid (465mg). This material was dissolved in hot absolute ethanol (10ml), succinic acid (184.6mg) added and the mixture aged at 55-60° for 1h, 20° for lh, then 5° for 2h. The resultant solid was filtered off, washed with a little ethanol, and dried under vacuum to give a cream solid (607mg). Crystallisation from ethanol (17ml) containing water (0.25ml) yielded the *title compound* (555mg, 73.9mCi, 59% radiochemical yield from potassium [^{14}C]cyanide) as a cream solid with m.p.165-167°. TLC (dichloromethane-ethanol-0.88 ammonia, 15:6:1), 99% radiochemical purity; HPLC: 5μ ODS2 column (15x0.46cm) eluted with acetonitrile-0.05M disodium hydrogen phosphate containing 1% v/v 0.5M dibutylammonium phosphate (1:4), flow rate = 1ml/min, R_t = 3.8min, chemical impurities 1% a/a (UV detection at 282nm), radiochemical purity 99%; specific activity 133μCi/mg, 55.3mCi/mmol; NMR data was similar to that for (1b) prepared by the alternative method decribed above).

2-[4-Formylamino-3-(1-methylpiperidine-4-carbonyl)phenyl]ethanesulphonic acid methylamide (17)

A solution of sodium periodate (2.11g, 9.85mmol) in water (100ml) was added to a suspension of 2-[3-(1-methylpiperidin-4-yl)-1H-indol-5-yl]ethanesulphonic acid methylamide hydrochloride (3a) (1.658g, 4.46mmol) in methanol (50ml) to give a pale yellow solution which was stored at 20° for 67h. A further portion of sodium periodate (225mg, 1.05mmol) in water (5ml) was then added and the mixture stirred for a further 1.5h. The solution was poured into saturated aqueous potassium carbonate (150ml), extracted with ethyl acetate (2x100ml) and the combined extracts dried and evaporated. The residual foam (1.653g) was purified by chromatography over silica gel using dichloromethane-ethanol-0.88 ammonia (70:8:1) as eluent. The ketone formed a cream coloured solid (1.242g, 76%) which was combined with similar material from a previous synthesis (174mg) and crystallised from ethyl acetate to give pure *title compound* (1.175g) as a white solid with m.p. 148-150°. δ_H (250MHz, DMSO-d_6) 10.90 and 8.43 (2H, br, CHO), 8.33 (1H, br d, NHCHO), 7.97 (1H, d, ArH), 7.55 (1H, dd, ArH), 7.05 (1H, br s, ArH), 2.64 (3H, br s, CH_3SO_2), 2.20 (3H, s, piperidinyl NCH_3). Found: C, 55.4; H, 6.9; N, 11.1; $C_{17}H_{25}N_3O_4S$ requires C, 55.6; H, 6.9; N, 11.4%.

2-[3-(1-Methylpiperidin-4-yl)-1H-[2-^{14}C]-indol-5-yl]ethanesulphonic acid methylamide hydrochloride (3b)

A solution of potassium [^{14}C]cyanide (73.0mg, 61.24mCi) in ethanol-water (19:1; 10ml) was added to 2-[4-formylamino-3-(1-methylpiperidine-4-carbonyl)phenyl]ethanesulphonic acid methylamide

(17) (400mg, 1.089mmol) and the mixture stirred at 20° for 4h to give a clear, pale yellow solution. Solvent was removed under vacuum, the residue dissolved in acetic acid (5ml) and tetrahydrofuran (3ml), cooled in an ice bath and treated with sodium borohydride (247mg, 6.5mmol), added in portions over 30min. After stirring for a further 30min at 5° the mixture was quenched with 2N hydrochloric acid (5ml) and allowed to stand at -20° for 16h. The solution was neutralised with 5M sodium hydroxide then added to saturated aqueous potassium carbonate (80ml) and extracted with ethyl acetate (2x75ml). Evaporation of the combined, dried extracts gave a foam which was purified by chromatography over silica gel using dichloromethane-ethanol-0.88 ammonia (75:8:1) as eluent. The resulting [^{14}C]GR85548 free base was redissolved in methanolic hydrogen chloride (10ml; from acetyl chloride (0.5ml) and methanol) and concentrated under vacuum to give the hydrochloride salt as a fawn solid (346mg, 85%). This material was crystallised from absolute ethanol (4ml)-water (1ml) and allowed to age at 20° for lh and 5° for 2.5h. The solid was filtered off and dried under vacuum to give the *title compound* as a white solid (272mg, 41.4mCi, 67% radiochemical yield). M.p. 239-242°. TLC (dichloromethane-ethanol-0.88 ammonia, 20:6:1), 99% radiochemical purity; HPLC: 3μ nitrile column (15x0.46cm) eluted with acetonitrile-isopropanol-triethylammonium phosphate buffer (4:18:78) (buffer prepared by diluting 85% phosphoric acid (68ml) to 1 litre with water, adjusting to pH2.5 with triethylamine and diluting 10ml of this solution to 1 litre with water), flow rate =0.8ml/min, R_t = 7.6min, chemical impurities 0.7% a/a (UV detection at 225nm), radiochemical purity 99%; specific activity 152μCi/mg, 56.8mCi/mmol; δ_H (250Mhz, DMSO-d_6) 7.61 (1H, s, ArH), 7.31 (1H, d, ArH), 7.14 (1H, br, NHCH=), 7.04 (1H, q, CH_3NHO_2S), 7.01 (1H, dd, ArH), 2.79 (3H, s, piperidinyl NCH_3), 2.65 (3H, d, CH_3NH).

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