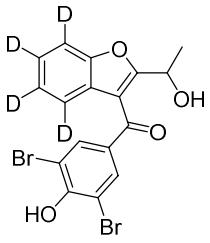
CLAIMS

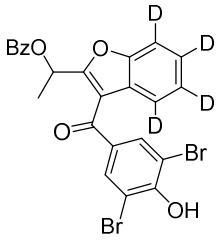
WHAT IS CLAIMED IS:

1. A process for the preparation of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1):



(Compound 1),

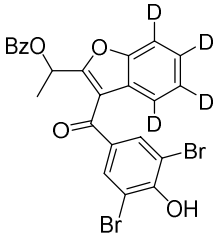
comprising contacting a compound with the structure:



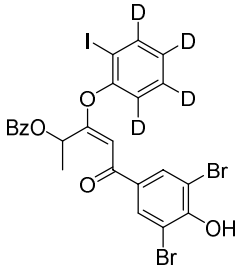
with cesium carbonate in the presence of a solvent.

2. The process of claim 1, wherein the solvent is selected from methanol, ethanol, isopropanol, butanol, water, acetone, acetonitrile, dimethylformamide, dimethyl sulfoxide, N-methyl-2-pyrrolidone, acetic acid, and combinations thereof.

3. The process of claim 1 or claim 2, wherein the compound with the structure:



is prepared by a process comprising contacting a compound with the structure:

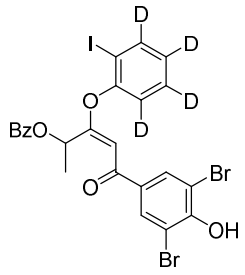


with a base and palladium catalyst in the presence of a solvent.

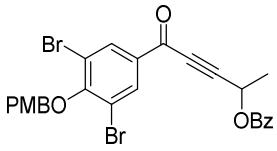
4. The process of claim 3, wherein the base is selected from potassium carbonate, silver carbonate, sodium carbonate, cesium carbonate, sodium bicarbonate, triethylamine, diisopropylethylamine, 1,8-diazabicyclo(5.4.0)undec-7-ene, and 1,4-diazabicyclo[2.2.2]octane, the palladium catalyst is selected from $Pd(dppf)Cl_2$, $PdCl_2$, $Pd(OAc)_2$, $Pd(Ph_3P)_4$, $Pd_2(dba)_3$, and Pd/C, and the solvent is selected from dimethyl

sulfoxide, dimethylformamide, N-methyl-2-pyrrolidone, acetone, acetonitrile, sulfolane, tetrahydrofuran, and toluene.

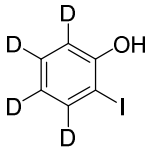
5. The process of claim 3 or claim 4, wherein the compound with the structure:



is prepared by a process comprising contacting a compound with the structure:



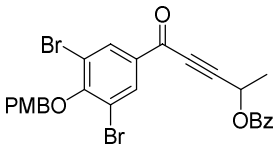
with a compound with the structure:



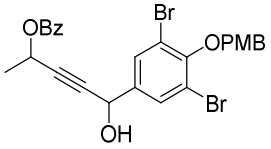
and potassium phosphate in the presence of a solvent followed by contact with trifluoroacetic acid.

6. The process of claim 5, wherein the solvent is selected from dichloromethane, chloroform, acetonitrile, toluene, ethyl acetate, and tetrahydrofuran.

7. The process of claim 5 or claim 6, wherein the compound with the structure:

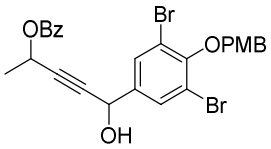


is prepared by a process comprising contacting a compound with the structure:

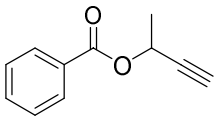


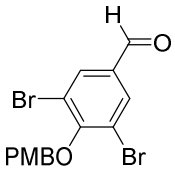
with sodium bicarbonate, potassium bromide, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), and sodium hypochlorite.

8. The process of claim 7, wherein the compound with the structure:



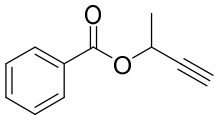
is prepared by a process comprising contacting a compound with the structure:

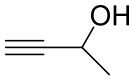
 with a compound with the structure:

 and a base in the presence of a solvent.

9. The process of claim 8, wherein the base is selected from lithium diisopropylamide, LiHMDS, NaHMDS, KHMDS, t-BuOK, t-BuONa, t-BuOLi, and NaH, and the solvent is selected from tetrahydrofuran, 2-methyltetrahydrofuran, dioxane, and toluene.

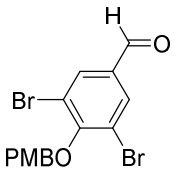
10. The process of claim 8 or claim 9, wherein the compound with the structure:

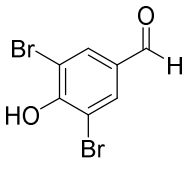
 is prepared by a process comprising contacting a compound with the structure:

 with benzoyl chloride and a base in the presence of a solvent.

11. The process of claim 10, wherein the base is selected from pyridine, potassium carbonate, sodium hydroxide, triethylamine, diisopropylethylamine, 1,8-diazabicyclo(5.4.0)undec-7-ene, and 1,4-diazabicyclo[2.2.2]octane, and lutidine and the solvent is selected from dichloromethane, tetrahydrofuran, 2-methyltetrahydrofuran, acetonitrile, dimethylformamide, dimethyl sulfoxide, and N-methyl-2-pyrrolidone.

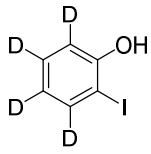
12. The process of claim 8 or claim 9, wherein the compound with the structure:

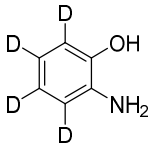
 is prepared by a process comprising contacting a compound with the structure:

 with 4-methoxybenzyl chloride and a base in the presence of a solvent.

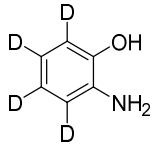
13. The process of claim 12, wherein the base is selected from potassium carbonate, sodium hydride, sodium carbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, triethylamine, diisopropylethylamine, and pyridine; and the solvent is selected from acetonitrile, dichloromethane, chloroform, tetrahydrofuran, 2-methyltetrahydrofuran, dimethylformamide, dimethyl sulfoxide, and N-methyl-2-pyrrolidone.

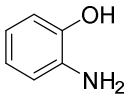
14. The process of claim 5 or claim 6, wherein the compound with the structure:

 is prepared by a process comprising contacting a compound with the structure:

 with sodium nitrite, potassium iodide, and toluenesulfonic acid.

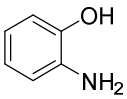
15. The process of claim 14 , wherein the compound with the structure:

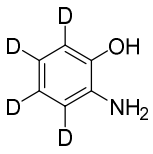
 is prepared by a process comprising contacting a compound with the structure:

 with 10% platinum on carbon and deuterium oxide.

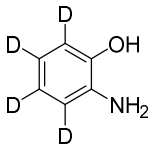
16. A process for the preparation of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), comprising:

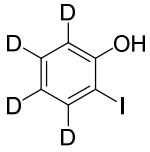
A) the reaction of a compound with the structure:

 with 10% platinum on carbon and deuterium oxide to produce a compound with the structure:

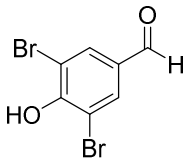
;

B) followed by the reaction of the compound with the structure:

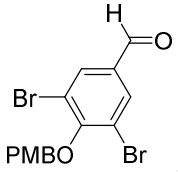
 with sodium nitrite, potassium iodide, and toluenesulfonic acid to produce a compound with the structure:

;

C) the reaction of a compound with the structure:

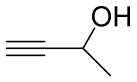


with 4-methoxybenzyl chloride and potassium carbonate to produce a compound with the structure:

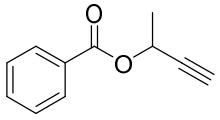


;

D) the reaction of the compound with the structure:

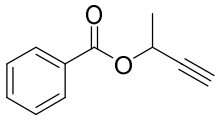


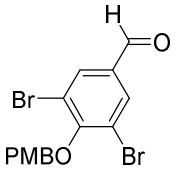
with benzoyl chloride and pyridine to produce a compound with the structure:



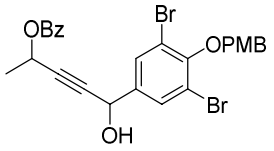
;

E) followed by the reaction of the compounds with the structures:



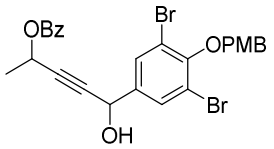
and 

with lithium diisopropylamide to produce a compound with the structure:

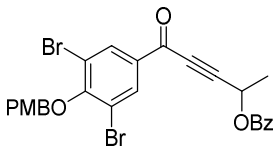


;

F) followed by the reaction of the compound with the structure:

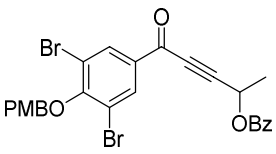
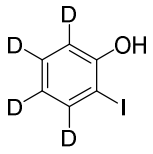


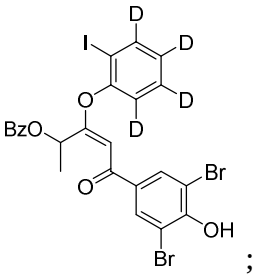
with sodium bicarbonate, potassium bromide, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), and sodium hypochlorite to produce a compound with the structure:



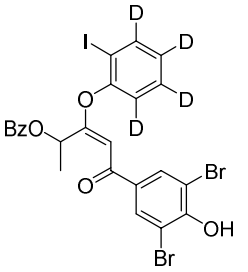
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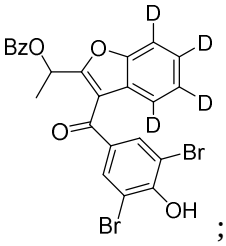
G) followed by the reaction of the compounds with the structures:

 and  and potassium phosphate, followed by contact with trifluoroacetic acid to produce a compound with the structure:

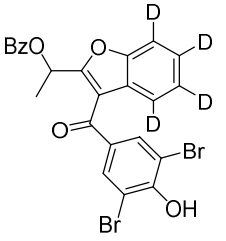
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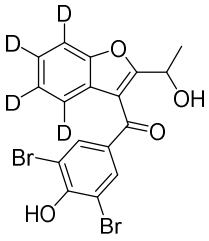
H) followed by the reaction of the compound with the structure:

 with potassium carbonate and $Pd(dppf)Cl_2$ to produce a compound with the structure:

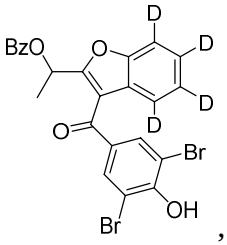
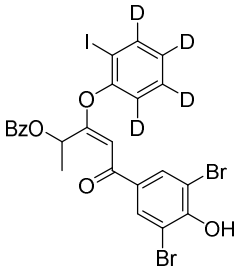
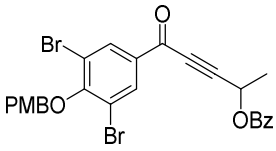
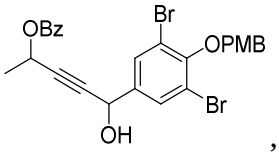
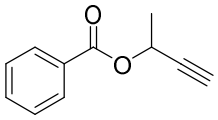
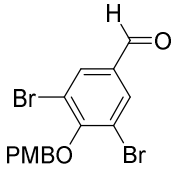
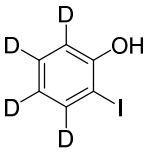
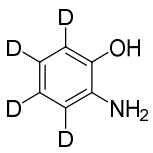
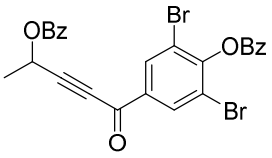
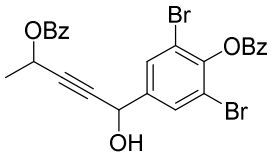
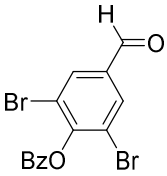
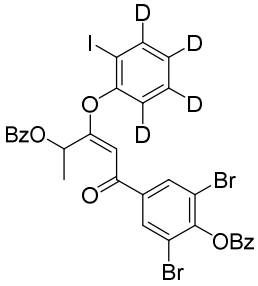
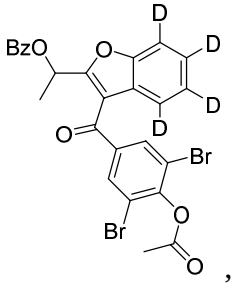
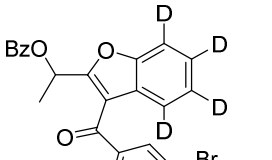
;

I) followed by the reaction of the compound with the structure:

 with cesium carbonate to produce a compound with the structure:

 (Compound 1).

17. A compound having a structure selected from:


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; or a pharmaceutically acceptable salt thereof.