



**Table 1.** Radiochemical yields and purities of [ $^{18}\text{F}$ ]butyrophenone neuroleptics

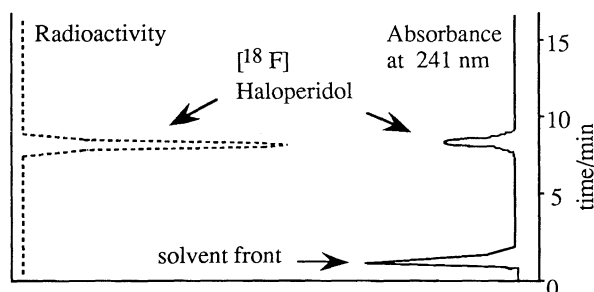
Run	Product (precursor)	Radiochemical	Radiochemical	Chemical	Reaction temp	Reaction time	Total synthesis
		yield/%	purity/%	purity/%	°C	min	time/min
1	[ $^{18}\text{F}$ ]haloperidol (nitrohaloperidol)	21	99	99	160	30	90
2	[ $^{18}\text{F}$ ]haloperidol (nitrohaloperidol)	11	99	99	160	20	80
3	[ $^{18}\text{F}$ ]haloperidol (nitrohaloperidol)	9	99	99	160	10	70
4	[ $^{18}\text{F}$ ]haloperidol (nitrohaloperidol)	1	99	99	150	5	65
5	[ $^{18}\text{F}$ ]spiperone (nitrospiperone)	19	99	99	160	20	80
6	[ $^{18}\text{F}$ ]spiperone (nitrospiperone)	1	99	99	150	5	65

nitrohaloperidol : 1-[4(4-Nitrophenyl)-4-oxobutyl]-4-(4'-chlorophenyl)-4-hydroxypiperidine

nitrospiperone : 8-[4-(4-nitrophenyl)-4-oxobutyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one

We then applied our reported purification method<sup>9</sup> for separating fluorobutyrophenone neuroleptics from their nitro precursors using a single HPLC column. The whole [ $^{18}\text{F}$ ]labeling reaction mixture was injected onto the preparative HPLC column [Eluent : MeCN:10mM NaOH = 50 : 50 (v/v), Asahipak ODP-50 (Shoko Co. Ltd., Tokyo),  $\phi$  21.5 mm x 250 mm + guard column  $\phi$  21.5 mm x 100 mm, flow rate 10 ml/min, positron monitor : TCS-R81 (Aloka Co. Ltd., Tokyo)] to isolate the labeled compound.

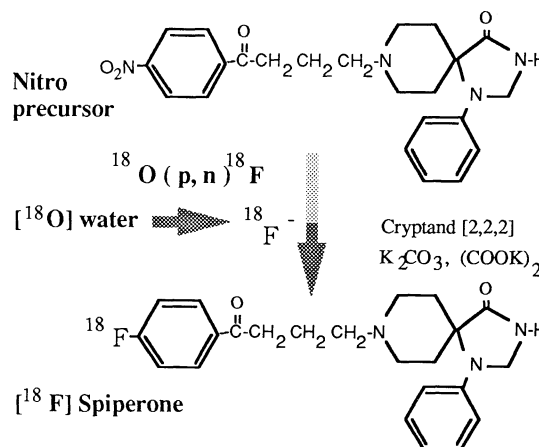
Analytical HPLC [Eluent : MeCN:10mM NaOH = 55 : 45 (v/v), Asahipak ODP-5,  $\phi$  4.6 mm x 150 mm + guard column  $\phi$  4.6 mm x 10 mm, flow rate 0.8 ml/min, UV 241 nm, radio analyzer : RLC-700 (Aloka)] was used to check the radiochemical and chemical purities of the purified hot products, using both UV (241 nm) and radioisotope detectors. As an example, the chromatographic pattern for separation of [ $^{18}\text{F}$ ]haloperidol is shown in Figure 2.



**Figure 2.** Analytical HPLC profile of [ $^{18}\text{F}$ ]haloperidol. (Eluent : MeCN:10mM NaOH = 50 : 50 (v/v), Asahipak ODP-50, 4.6 mm x 250 mm).

We synthesized [ $^{18}\text{F}$ ]haloperidol and [ $^{18}\text{F}$ ]spiperone from their nitro precursors as shown in Table 1. The total synthesis time was 60~95 min (drying-up : 20~30 min, fluorination : 5~30 min : purification : 35 min). The radiochemical yields were 1~21% [decay corrected] and both the radiochemical purity and chemical purity were 99% (no precursors were detected). The analytical values were remarkably high compared to previous products from the nitro-fluoro exchange reaction.

The simplicity of our synthetic method has allowed us to make a straightforward automated synthesis apparatus that is suitable for routine use. We are now applying this method to the synthesis of other high radiochemical purity  $^{18}\text{F}$ -labeled butyrophenone neuroleptics ([ $^{18}\text{F}$ ]N-methylspiperone, etc.) and other ligands for studying brain and cardiovascular functions.



**Figure 3.**

We believe our synthetic method will further promote the development of  $^{18}\text{F}$ -labeled tracers for PET.

#### References and Notes

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