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Bromo[^{18}F]fluorination of cyclohexenes: a method for the preparation of [^{18}F]fluorocyclohexanes

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Abstract

In an earlier report, we described an olefin halofluorination process that was used to label monosubstituted alkenes with fluorine-18 at the no-carrier-added level. In this report, we describe further studies on the radiohalofluorination of more highly substituted and more reactive alkenes, such as the cyclohexenes 1,4-diisopropylcyclohexene (DIPC), 1-methylcyclohexene (MeC) and pregnenolone (3β-hydroxy-5-pregnen-20-one). DIPC, MeC and pregnenolone were labeled with fluorine-18 in 30%, 26% and 35% radiochemical yields, respectively, within 15 min at 0 °C under no-carrier-added conditions. A comparison of the conditions required to obtain optimal yields for fluorine-18 radiohalofluorination with these trisubstituted cyclic alkene systems vs. the monosubstituted alkenes studied earlier, suggests that alkene systems with different degrees of alkyl substitution (and hence different reactivity towards electrophiles) will each require careful optimization of the reaction conditions.

Keywords: Bromo[^{18}F]fluorination; Cyclohexenes; Radiolabeling; NMR spectroscopy; Mass spectrometry

1. Introduction

Fluorine-18 ($t_{1/2}$ = 110 min) is a positron-emitting radionuclide that is widely employed for the labeling of radiopharmaceuticals used in positron emission tomography (PET). Despite its many favorable characteristics (small steric size, stable bonding to carbon, convenient half-life and ease of production), only a few chemical reactions are suitable for introducing fluorine-18 into radiopharmaceuticals at high specific activity [1]. Nucleophilic displacement utilizing [^{18}F]fluoride ion works well in aliphatic systems, where reactive halides and sulfonate esters can undergo substitution at unhindered sites, and in certain aromatic systems where nitro, trimethylammonium or dimethylsulfonium groups on electron-deficient aromatic rings can undergo substitution by a two-step addition–elimination process (for a comprehensive review, see Ref. [2]).

In an earlier report, we described an olefin halofluorination process that could be used to label alkenes with fluorine-18 at the no-carrier-added level [3]. Olefin halofluorination involves the in situ generation of a species with the character of a halogen fluoride by treatment of a solution of fluoride ion in acidic medium with a source of the electrophilic halogen, followed by subsequent addition of the elements of halogen fluoride across the olefin. In these earlier studies, we investigated the characteristics of this reaction with three monosubstituted olefins [allylbenzene (**1**), 1-hexene and propene] as model systems to assess the potential of halofluorination for fluorine-18 labeling purposes.

Because the addition of halogen fluoride to acyclic alkenes is governed by Markovnikov's rule, the principal adducts of these terminal alkenes were the 1-bromo-2-fluoro isomers. While it is difficult to use the halofluorination process to prepare primary fluoro compounds (those that are most readily prepared by S_N2 substitution), this addition reaction has an advantage in the preparation of compounds having fluorine situated at a secondary or tertiary position (those systems where S_N2 substitution would be most difficult).

In this report, we describe further studies on the radiohalofluorination of more highly substituted alkenes.

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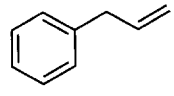
We find that these alkenes are, as expected, more reactive toward this electrophilic addition: as a result, reaction conditions must be carefully developed to obtain the efficient incorporation of [^{18}F]fluoride ion. These studies were prompted by our interest in using the halofluorination reaction to label steroids at the 11β and 6α positions [4]. As these rigid polycyclic steroid systems present some unique stereoelectronic problems, we will present a full report of our results on the halofluorination of steroids elsewhere. Hence, in this account, we present the results of halofluorination of three cyclic olefins, i.e. 1,4-diisopropylcyclohexene (**2**, DIPC), 1-methylcyclohexene (**3**, MeC) and pregnenolone (**4**, 3β-hydroxy-5-pregnen-20-one).



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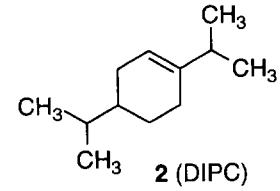

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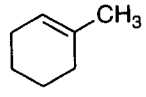
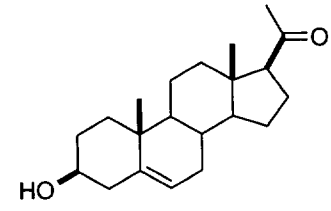


3 (MeC)



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2. Results and discussion

2.1. General characteristics of olefin halofluorination and radiohalofluorination

We have found that halofluorination reactions on the macroscopic scale generally proceed very well using pyridine poly(hydrogen fluoride) (HF/pyridine) as a source of fluoride, and with electrophilic halogen sources such as *N*-bromosuccinimide (NBS), 1,3-dibromo-5,5-dimethylhydantoin (DBH) and *N*-iodosuccinimide (NIS) in an inert solvent such as dichloromethane. However, at the tracer level, [^{18}F]fluoride ion produced from [^{18}O]H_2O target exists in the form of various metal fluorides which can have quite low reactivity [5]. With the terminal alkene model system, we obtained the best yields for radiohalofluorination using concentrated sulfuric acid as the source of acid, DBH as the halogen source and dichloromethane as solvent. While trifluoromethanesulfonic acid provided good yields of olefin halofluorination on the macroscopic scale, it gave very poor incorporation of fluorine-18 at the tracer level [3].

2.2. Temperature and alkene reactivity

Although we have not characterized the chemical species obtained by the mixing of HF and a source of electrophilic bromine, in terms of alkene addition reactions it has the reactivity of the interhalogen bromine fluoride (BrF), in which bromine behaves as the electrophile. Thus, under the usual circumstances, 'Br^+' attacks the alkene forming a bromonium ion intermediate, which is then attacked with some selectivity at the more highly substituted site by fluoride ion, giving the adduct favored by Markovnikov's rule. (Regioselectivity in electrophilic additions to cyclic alkenes also reflects the preference for diaxial addition – Fürst–Plattner rule [6].) The reactivity of BrF towards alkenes can be so great that control of the reaction can be difficult; Rozen and co-workers have used trace amounts of ethanol to moderate this reaction [7].

Since electrophilic bromine is more reactive towards alkenes of increased alkyl substitution, we anticipated that the cyclic trisubstituted alkenes studied here would be more reactive than the monosubstituted ones we studied previously. In fact, using the same conditions we employed with the terminal olefins (25 °C), we obtained yields of only 5% with the more substituted alkenes (cf. Table 1).

Table 1
Bromo[^{18}F]fluorination of allylbenzene (**1**), 1,4-diisopropylcyclohexene (DIPC, **2**) or 1-methylcyclohexene (MeC, **3**) [a]

Entry	Olefin	Temp. (°C)	Yield (%) after			(*n*) [b]
			3 min	5 min	10 min	
1	**1c** [c]	rt			32.0±8.8	(3)
2	**1**	0	5.9	5.2		
3	**2**	rt		4.1±3.2	3.3±1.2	(3)
4	**2** [d]	0	29.4±1.6	29.3±3.7	30.3±2.8	(3)
5	**2** [e]	0		28.3	27.1	
6	**2**	−10	8.8	17.5	27.7	
7	**2** [f]	−78			55.1	
8	**3**	0	30.5	30.4	25.7	

[a] Reactions were conducted with 0.5–10 mCi of [^{18}F]fluoride activity as described in the experimental details; the amounts of olefin, 1,3-dibromo-5,5-dimethylhydantoin (DBH) and H_2SO_4 in these reactions were 100, 50 and 10 μmol, respectively.

[b] Yields were measured by TLC using a radio TLC scanner and are given for individual reactions or as average yields with standard deviation for multiple reactions. The yields obtained by radio TLC analysis were the same as those obtained by isolation using Florisil column chromatography.

[c] From our previous report [3].

[d] One of these reactions was undertaken with smaller amounts (olefin/DBH/H_2SO_4, 25:25:5 μmol).

[e] The reaction was performed without a magnetic stirring bar; each reaction mixture was shaken by a Vortex mixer for 5 s before and after adding olefin.

[f] At −78 °C, there was no incorporation of F-18. The yield at 10 min was obtained after removing a Dry Ice/acetone bath and allowing the reaction vessel to warm slowly.

As model trisubstituted alkenes, we used 1,4-diisopropylcyclohexene (DIPC, **2**) and 1-methylcyclohexene (MeC, **3**), and for comparison with our earlier results, the monosubstituted alkene allylbenzene (**1**). As shown in Table 1 (entries 3–7), the halofluorination reaction with the cyclic trisubstituted alkene **2** was very sensitive to temperature. Although the yield at 25 °C was only 3%–4%, DIPC was labeled with fluorine-18 in 29% yield at 0 °C within 3 min under no-carrier-added conditions; the yield was unchanged at longer reaction times (entry 4). The reaction at −10 °C was slower than that at 0 °C, but reached the same level of completion (entry 6). At −78 °C the reaction did not proceed at all, but after removal of the Dry Ice acetone bath a 55% yield was obtained at 10 min (entry 7). Presumably, the reaction proceeded well at an intermediate temperature. For practical purposes, the optimum reaction temperature for DIPC (**2**) was 0 °C. The other trisubstituted alkene MeC (**3**) behaved in an almost identical fashion (entry 8). In contrast to the 0 °C optimum reaction temperature for the trisubstituted cyclic alkenes DIPC (**2**) and MeC (**3**), allylbenzene (**1**) underwent fluorine-18 radiolabeling by halofluorination best at 25 °C (entry 1); the yield at 0 °C was only ca. 6% (entry 2). Thus, alkenes of different structure and reactivity have different optimum conditions for halofluorination.

2.3. Stirring and tracer-scale conditions

As documented in our previous study [3], alkene bromofluorination on the macroscopic scale is a more robust reaction than at the tracer level scale. For example, bromofluorination of allylbenzene at the 8.46-mmol scale proceeded equally well at both −23 °C and 25 °C, whereas this was not the case at the tracer level (cf. Table 1, entries 1 and 2). In addition, we found that a wider range of acids could be used in the macroscopic-scale halofluorination, whereas only concentrated sulfuric acid sufficed at the tracer level. Not surprisingly, the 'physical' aspects of the reaction rather than just the 'chemical' ones, become important at the tracer level. In one case (Table 1, entry 5), radiohalofluorination reaction of DIPC (**2**) was performed at 0 °C without magnetic stirring, but the reaction vessel was shaken with a Vortex mixer for 5 s before and after DIPC (**2**) was added. The incorporation yield was 28% at 5 min and 27% at 10 min, the same as that when magnetic stirring was used (entry 4).

The issue of stirring is significant as these reactions are heterogeneous; sulfuric acid (the only acid that was satisfactory in our hands for tracer-scale radiohalofluorination) is not soluble in the dichloromethane solvent. Acid-induced decomposition of the alkene competes with the bromofluorination process, a factor that may underlie the different temperature optima for halofluorination of the different alkenes. Rapid stirring to disperse the sulfuric acid is essential for the reaction, as the acid is required to generate HF from the metal fluoride salts and ensure its reaction with 1,3-dibromo-5,5-dimethylhydantoin (DBH) to produce the interhalogen species.

2.4. Halofluorination of pregnenolone

We have performed halofluorination reactions with the more complex alkene pregnenolone (**4**). On the macroscopic scale, halofluorination provided three major isomers, 5α-bromo-6β-fluoro-3β-hydroxypregnan-20-one (**7a**, bromide attacked from the α-face and anti-Markovnikov addition), 6β-bromo-5α-fluoro-3β-hydroxypregnan-20-one (**7b**, bromide attacked from the β-face and Markovnikov addition) and 6α-bromo-5β-fluoro-3β-hydroxypregnan-20-one (**7c**, bromide attacked from the α-face and Markovnikov addition). The detailed chemistry of this halofluorination reaction will be published separately. However, the yield of the radiohalofluorination reaction was 16% at 0 °C after 15 min, while the yields were low both at room temperature and −23 °C (Table 2).

2.5. Stoichiometry

Model compounds such as the alkenes DIPC (**2**), MeC (**3**) and allylbenzene (**1**) are inexpensive and can be used in vast excess to obtain high yields in radiolabeling reactions performed at the tracer level. However, this is not usually the case with complex synthetic precursors, as might be used in the radiolabeling of drugs and hormones when only limited quantities may be available. In addition, the radiopharmaceutical can more readily be obtained at high effective specific activity

Table 2
Bromo[^{18}F]fluorination of pregnenolone (**4**) [a]

Olefin/DBH/H_2SO_4 (μmol)	Temp. (°C)	Yield (%) after			(*n*) [b]
		1 min	5 min	15 min	
100:50:10	rt		4.3	5.1	(2)
	0	9.6±3.8	10.1±2.2	15.8±5.3	(4)
	−23		2.8	4.7	
50:50:10	0			34.5	(2)
25:25:5	0	6.3	7.3	26.0	

[a] Reactions were conducted with 0.5–10 mCi of [^{18}F]fluoride activity as described in the experimental details. All reactions were performed with a magnetic stirring bar and the reaction mixture was shaken by a Vortex mixer for 5 s before and after adding alkene.

[b] Yields were measured by TLC using a radio TLC scanner and are given for individual reactions or as average yields with standard deviation for multiple reactions. The yields obtained by radio TLC analysis were the same as those obtained by isolation using Florisil column chromatography.

[8] when only small quantities of organic precursor are used. Thus, there are significant advantages if tracer-scale radiolabeling can be performed efficiently with small amounts of organic precursors. In the case of the bromofluorination reaction which we have studied here, when the amount of reagents were reduced from 100 μmol to 25 μmol of DIPC (2), from 50 μmol to 25 μmol of DBH and from 10 μmol to 5 μmol of sulfuric acid, a similar yield was obtained. When the reaction with pregnenolone was run with 50 μmol of steroid, 50 μmol of DBH and 5 μmol of sulfuric acid, an improved yield of 35% was obtained. This suggests that further optimization of stoichiometry may be possible.

We hope that the documentation of improved methods for the radiobromofluorination of more highly substituted and complex alkenes will encourage the use of this reaction in the preparation of fluorine-18 labeled radiopharmaceuticals at the no-carrier-added level.

3. Experimental details

Flash chromatography was performed according to Still et al. [9] using Woelm silica gel (0.040–0.063 mm). ^{1}H NMR spectra were recorded at 300 MHz using a General Electric QE-300 (300 MHz) spectrometer and are reported in parts per million (ppm) downfield from internal tetramethylsilane. ^{19}F NMR spectra were recorded at 376.3 MHz using a Varian Unity spectrometer and are reported in ppm downfield from internal fluorotrichloromethane. Mass spectra were obtained on Finnigan MAT CH5 and VG 70-VSE spectrometers for EI and CI spectra, respectively. Elemental analyses were performed by the Microanalytical Service, School of Chemical Sciences, University of Illinois.

3.1. 2-Bromo-1-fluoro-1,4-diisopropylcyclohexane and isomers (5)

This material was prepared according to our previous procedure (method A) [3]. 1,3-Dibromo-5,5-dimethylhydantoin (DBH) (858 mg, 3.0 mmol), CH_2Cl_2 (15.0 ml), HF/pyridine (190 mg, 6.0 mmol) and 1,4-diisopropylcyclohexene (DIPC, **2**) (832 mg, 5.0 mmol) were used. The reaction time was 15 min. The crude product **5** (1.30 g, 98%) was obtained as a colorless oil after work-up. Bulb-to-bulb distillation of **5** gave a colorless oil (950 mg, 72%). The ^{1}H NMR spectra of the crude and distilled products were almost the same and showed them to be, as expected, a mixture of all possible stereo and regio isomers. Bromofluorides **5** were analyzed as the mixture. MS (CI) *m/z* (%): 266 ($M^+ + 1$, 1); 264 ($M^+ + 1$, 1); 245 (9); 243 (7); 231 (4); 229 (4); 183 (14); 165 (100); 109 (58). Analysis: Calc. for $C_{12}H_{22}BrF$: C, 54.35; H, 8.36; F, 6.95%. Found: C, 54.49; H, 8.29; F, 6.95%.

3.2. 2-Bromo-1-fluoro-1-methylcyclohexane (6)

This material was prepared according to our previous procedure (method A) [3]. DBH (858 mg, 3.0 mmol), CH_2Cl_2 (15.0 ml), HF/pyridine (190 mg, 6.0 mmol) and 1-methylcyclohexene (MeC, **3**) (481 mg, 5.0 mmol) were used. The reaction time was 15 min. The product was obtained as a colorless oil **6** by bulb-to-bulb distillation (305 mg, 31%, not optimized). The ^{1}H and ^{19}F NMR spectra of **6** showed the Markovnikov addition product as the major component, together with a trace amount of the anti-Markovnikov product. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.35–2.30 (m, 8); 1.51 (d, 3, J=22.5 Hz, CH_3); 4.20 (td, 1, J=7.5, 4.0 Hz, CHBr) ppm. MS (EI, 70 eV, off-scale) *m/z* (%): 196 ($M^+ + 1$, 15); 195 (M^+, 20); 194 ($M^+ + 1$, 19); 193 (M^+, 18); 175 (11); 134 (72); 132 (69); 115 (100). Analysis: Calc. for $C_7H_{12}BrF$: C, 43.10; H, 6.20; F, 9.74%. Found: C, 43.23; H, 6.36; F, 9.62%.

3.3. 5α-Bromo-6β-fluoro-3β-hydroxy-pregnan-20-one (7a), 6β-bromo-5α-fluoro-3β-hydroxy-pregnan-3β-ol-20-one (7b) and 6α-bromo-5β-fluoro-3β-hydroxy-pregnan-3β-ol-20-one (7c)

This material was prepared according to our previous procedure (method A) [3]. DBH (170 mg, 0.6 mmol), CH_2Cl_2 (5.0 ml), HF/pyridine (38 mg, 1.2 mmol) and pregnenolone (**4**) (316 mg, 1.0 mmol) were used. The reaction time was 15 min. After work-up, the crude mixture consisted of three components (the ratio of 7a:7b:7c based on ^{1}H NMR was 34:37:29). Flash column chromatography (silica gel, 30% EtOAc/hexane) of this mixture provided a mixture of **7a** and **7b** (250 mg, 60%, white solid) and **7c** (120 mg, 29%, white solid). Compounds **7a** and **7b** were analyzed as the mixture. ^{1}H NMR (300 MHz, $CDCl_3$) selected data for **7a**, δ: 0.63 (s, 3, C18-CH_3); 1.23 (d, 3, J=4.6 Hz, coupled with C6β-F through space, C19β-CH_3); 2.11 (s, 3, $COCH_3$); 4.32–4.45 (m, 1, C3α-H_{ax}); 4.80 (dt, 1, J=46.4, 2.5 Hz, C6α-H_{eq}) ppm. ^{19}F NMR (376.3 MHz, $CDCl_3$) δ: −165.63 (tdd, 1, J=48.1, 14.9, 3.3 Hz, C6β-F) ppm. ^{1}H NMR (300 MHz, $CDCl_3$) selected data for **7b**, δ: 0.65 (s, 3, C18-CH_3); 1.31 (s, 3, C19β-CH_3); 2.11 (s, 3, $COCH_3$); 3.90–4.03 (m, 1, C3α-H_{ax}); 4.07–4.13 (m, 1, C6α-H_{eq}) ppm. ^{19}F NMR (376.3 MHz, $CDCl_3$) δ: −146.60 (d, 1, J=41.2 Hz, C5α-F) ppm. MS (CI) *m/z* (%): 417 ($M^+ + 1$, 10); 415 ($M^+ + 1$, 14); 399 (30); 397 (64); 395 (39); 379 (22); 377 (19); 335 (83); 315 (86); 297 (100); 279 (14). Compound **7c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.61 (s, 3, C18-CH_3); 1.03 (s, 3, C19β-CH_3); 1.18–2.28 (m, 17); 2.12 (s, 3, $COCH_3$); 2.47–2.63 (m, 3); 4.11 (b s, 1, C3α-H_{eq}); 4.57 (ddd, 1, J=12.8,

10.2, 4.9 Hz, C6β-H_{ax}) ppm. ^{19}F NMR (376.3 MHz, $CDCl_3$) δ: −149.64 (dt, 1, J=47.0, 9.0 Hz, C5β-F) ppm. MS (CI) m/z (%): 417 (M^++1, 14); 415 (M^++1, 26); 399 (53); 397 (66); 395 (22); 379 (23); 377 (23); 335 (23); 315 (71); 297 (100); 279 (16). Analysis: Calc. for $C_{21}H_{32}BrFO_2$: C, 60.74; H, 7.77; Br, 19.22; F, 4.57%. Found: C, 61.02; H, 7.82; Br, 19.04; F, 4.49%.

3.4. General radiochemical methods

Fluorine-18 was prepared from [^{18}O]H_2O by the [^{18}O(p,n)^{18}F] reaction in either a Havar/stainless steel or an all-titanium target [5], and the indicated quantity of radioactivity was dried as reported previously [3]. All reactions were performed at the no-carrier-added level. Transfer of conc. sulfuric acid (0.27 or 0.53 μl, 5 or 10 μmol) with a 5 or 10 μl Hamilton syringe provided the best results.

3.5. General procedure for bromo[^{18}F]fluorination

[^{18}F]Fluoride activity (0.5–10 mCi) in water (10–100 μl) was placed in a polyethylene reaction tube and evaporated to dryness at 80 °C under a gentle stream of nitrogen by azeotropic distillation using acetonitrile (100–200 μl). The reaction vessel was cooled to the indicated reaction temperature. Then, DBH (25–50 μmol), 400 μl CH_2Cl_2 and 5–10 μmol H_2SO_4 were added, followed by 25–100 μmol of the alkene. The reactions were stirred with a small Teflon-coated magnetic stirring bar, and the progress of the incorporation of radioactivity into the organic fraction was monitored by radio TLC. In the case indicated, the reaction mixture was agitated by a Vortex mixer for 5 s before and after adding the olefin. Products were isolated by column chromatography – the reaction mixture was transferred to a column of silica gel or Florisil (2.0×0.4 cm), which was washed with an additional 1–2 ml of CH_2Cl_2/EtOAc (1:1) to elute the halofluorination products. Yields are given in Tables 1 and 2.

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References

[1] M.S. Berridge and T.J. Tewson, *Appl. Radiat. Isot., 37* (1986) 685; O. Solin, J. Bergman, M. Haaparanta and A. Reissell, *Appl. Radiat. Isot., 39* (1988) 1065.
[2] M.R. Kilbourn, *Fluorine-18 Labeling of Radiopharmaceuticals,* National Academy Press, Washington, DC, 1990.
[3] D.Y. Chi, D.O. Kiesewetter, J.A. Katzenellenbogen, M.R. Kilbourn and M.J. Welch, *J. Fluorine Chem., 31* (1986) 99.
[4] S.J. Brandes and J.A. Katzenellenbogen, *Mol. Pharm., 32* (1987) 319; T.J. de Groot, *Ph.D. Dissertation,* Rijks University, Groningen, 1993.
[5] M.R. Kilbourn, J.T. Hood and M.J. Welch, *Int. J. Appl. Radiat. Isot., 35* (1984) 599; M.R. Kilbourn, P.A. Jerabek and M.J. Welch, *Int. J. Appl. Radiat. Isot., 36* (1985) 327.
[6] E.L. Eliel, *Stereochemistry of Carbon Compounds,* McGraw-Hill, New York, 1962, p. 230.
[7] S. Rozen and M. Brand, *J. Org. Chem., 50* (1985) 3342.
[8] S.G. Senderoff, K.D. McElvany, K.E. Carlson, D.F. Heiman, J.A. Katzenellenbogen and M.J. Welch, *Int. J. Appl. Radiat. Isot., 33* (1982) 545.
[9] W.C. Still, M. Kahn and A. Mitra, *J. Org. Chem., 43* (1978) 2923.