Available online at www.sciencedirect.com
ScienceDirect
Journal of Fluorine Chemistry 128 (2007) 127–132
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Radical scavengers: A practical solution to the reproducibility issue in the fluoridation of diaryliodonium salts

Michael A. Carroll [a,*], James Nairne [b], Graham Smith [a], David A. Widdowson [c]

[a] School of Natural Sciences – Chemistry, Newcastle University, Newcastle upon Tyne NE1 7RU, UK
[b] GE-Healthcare, The Grove Centre, White Lion Road, Amersham, Buckinghamshire HP7 9LL, UK
[c] Department of Chemistry, Imperial College, London SW7 2AY, UK

Received 9 October 2006; received in revised form 26 October 2006; accepted 27 October 2006
Available online 6 November 2006

Abstract

The addition of radical scavengers to the fluoridation of diaryliodonium salts was demonstrated to improve significantly both the reproducibility of the process and the material yield of the desired fluoroarene products. It was also established that the selectivity of the process was not influenced by the presence of the radical scavengers. TEMPO and galvinoxyl were found to be the most suitable radical scavengers in the fluoridation process allowing the methodology to be used routinely for the first time.

Keywords: Fluorinated aromatics; Fluorine-18; Fluorination; Hypervalent iodine

1. Introduction

Iodine, like the other halogens, is found typically in its monovalent form (oxidation state: −1). However due to its large size and polarisability, it is able to form stable polycoordinate, multivalent compounds. Compounds of this type, containing hypervalent iodine, have been known for over a century and received considerable attention. The ability of these compounds to act as both selective reagents and intermediates has formed the basis of this interest [1–5].

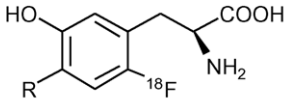
Our interest in the most numerous member of this group, the diaryliodonium salts, arose from the demonstration that they are suitable precursors for the formation of fluoroarenes by the action of fluoride ion [6–8]. The use of this methodology in the production of fluorine-18 labelled radiopharmaceuticals would have distinct advantages over conventional electrophilic procedures, which employ molecular $[^{18}F]F_2$ and derivatives, as $[^{18}F]$fluoride can be produced in higher amounts and higher specific radioactivity by several orders of magnitude [9]. This is an important consideration as these materials are required at very high specific radioactivity as receptor radioligands in clinical research using positron emission tomography (PET). PET is an imaging technique for the absolute measurement, *in vivo*, of positron emitters, enabling their pharmacokinetics and biodistribution to be elucidated by non-invasive means. In addition, unlike conventional nucleophilic aromatic substitution, the process places little or no restriction on the nature of aromatic substituents or their position providing a verstaile method for the formation of fluoroarenes.

These benefits have resulted in much recent interest in diaryliodonium salts as precursors to fluorine-18 arenes [10–16], however we, and others [12,16], have observed that the fluoridation results can be extremely variable, particularly in the case of electron-rich diaryliodonium salts. Despite the potential benefits the approach has for the introduction of fluorine-18 into aromatic systems the associated lack of reproducibility has severely limited the development and application of this approach to the production of fluorine-18 labelled radiopharmaceuticals.

We now wish to report a modification to the fluoridation procedure which addresses the question of reproducibility and also dramatically increases the material yield of the process.

* Corresponding author. Tel.: +44 191 2227074; fax: +44 191 2226929.
E-mail address: m.a.carroll@ncl.ac.uk (M.A. Carroll).

0022-1139/$ – see front matter © 2006 Published by Elsevier B.V.
doi:10.1016/j.jfluchem.2006.10.018



1 R = OH, L-6-[^{18}F]fluoroDOPA

2 R= H, L-6-[^{18}F]fluoro-*m*-tyrosine

Fig. 1. Fluorine-18 labelled phenethylamine derivatives.

2. Results and discussion

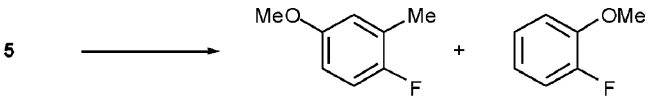
Phenethylamines form an extremely important class of biologically active compounds, of particular interest are those that possess neurological activity [17] and as such their fluorinated derivatives have immense potential as radiopharmaceuticals (Fig. 1).

L-6-[^{18}F]FluoroDOPA (**1**) is a well established example of this and is a radioligand for the study of brain dopaminergic neuron density in movement disorders, such as Parkinson's disease [18,19]. In addition 6-[^{18}F]fluoro-*m*-tyrosine (**2**) has proven a useful alternative to L-6-[^{18}F]-fluoroDOPA as it remains a substrate for aromatic L-amino acid decarboxylase (producing the phenethylamine derivatives) yet is not subject to methylation by catecholamine-*O*-methyltransferase allowing improved contrast in PET images [20] (Scheme 1).

We proposed iodonium salt **5** as a suitable model compound for studies towards a range of fluorinated phenethylamines as (a); the 2-methyl group effectively mimics the ethylamine side chain of the targets and (b); the 4-methoxy substitution results in an electron-rich aromatic ring which is also consistent with the desired structures. The electronic nature of the aromatic rings is known to influence the outcome of nucleophilic substitution [21–23] and the second ring (2-methoxyphenyl [24]) is present to balance this controlling property allowing the formation of all potential products in sufficient quantities to aid detection and therefore the understanding of the process. The preparation of **5** began with the oxidation of 2-iodoanisole, **3** using sodium perborate in acetic acid [25] which provided the iodobisacetate, **4** in good yield (67%). The addition of 3-methylanisole, in the presence of TFA gave the target iodonium salt **5** in 93% yield according to our standard procedure [26].

Initial studies on the fluoridation of iodonium salt **5** (Table 1) gave the expected ring selectivity (effectively equal quantities of **6** and **7**) and further highlighted the lack of reproducibility with DMF providing the, only slightly, best results. Optimisation of this process was therefore a key goal towards the high specific activity production of [^{18}F]fluorophenethylamine derivatives.

Table 1
Fluoridation of iodonium salt **5**



6 **7**

Solvent[a]	Yield[b]	**6**:**7**
MeCN	<5%	1:1
Me_2SO	<5%	1:1
DMF	<5%	1.1:1
DMAC	<5%	1:1

[a] CsF (2 equiv.), 90 °C, 1.5 h.
[b] By ^{19}F NMR relative to the internal standard $PhCF_3$.

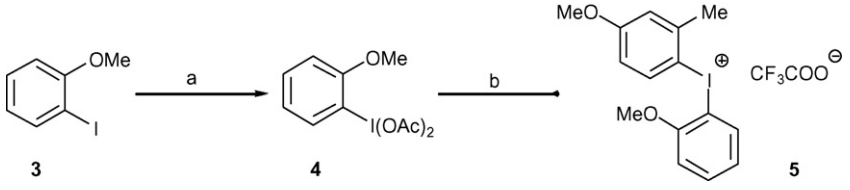
Table 2
Fluoridation of **5** in the presence of radical scavengers

Scavenger	Yield range[a,b] (%)	Average yield[c] (%)	**6**:**7**
4-Aminobenzoic acid	8–25	16	1.3:1
BHT	14–28	21	1.3:1
1,1-Diphenylethylene	20–28	23	1.3:1
Galvinoxyl	22–29	26	1.3:1
Gentisic acid	6–12	9	1.2:1
Hydroquinone	<5	n/a	1:1
TEMPO	24–26	25	1.3:1
Thiophenol	13–28	19	1.2:1
DL-α-Tocopherol	10–28	16	1.2:1

[a] CsF (2 equiv.), DMF, 90 °C, 1.5 h, scavenger (10 mol%).
[b] By ^{19}F NMR relative to the internal standard 3-trifluoromethylanisole.
[c] Average of three runs.

It was decided to improve both the yield and reproducibility of the fluoridation process by minimising the influence of any competing side reactions that may be occuring. Hypervalent iodine compounds are known to undergo numerous reaction pathways, of which one major pathway is due to the homolytic fisson of the aryl iodine bond generating aromatic radicals that may undergo further, undesired, chemistry. A study of the crude fluoridation reaction mixtures supported this premise as a random range of protio-products (e.g. anisole derivatives) and biaryl materials was evident in significant amounts by GC–MS analysis.

In order to minimise the potential disruption of the fluoridation process, by *in situ* generated radicals, a range of radical scavengers was tested as a method of control. The radical scavengers (Fig. 2) were selected based on their previously demonstrated ability in this role. These included 4-aminobenzoic acid [27], 2,6-di-*tert*-butyl-4-methylphenol (BHT) [28,29], 1,1-diphenylethylene [30], galvinoxyl [31–33], gentisic acid



3 **4** **5**

Scheme 1. (a) $NaBO_3{\cdot}4H_2O$, AcOH, 45 °C, 67% and (b) TFA, 3-methylanisole, CH_2Cl_2, −30 °C to RT, 93%.

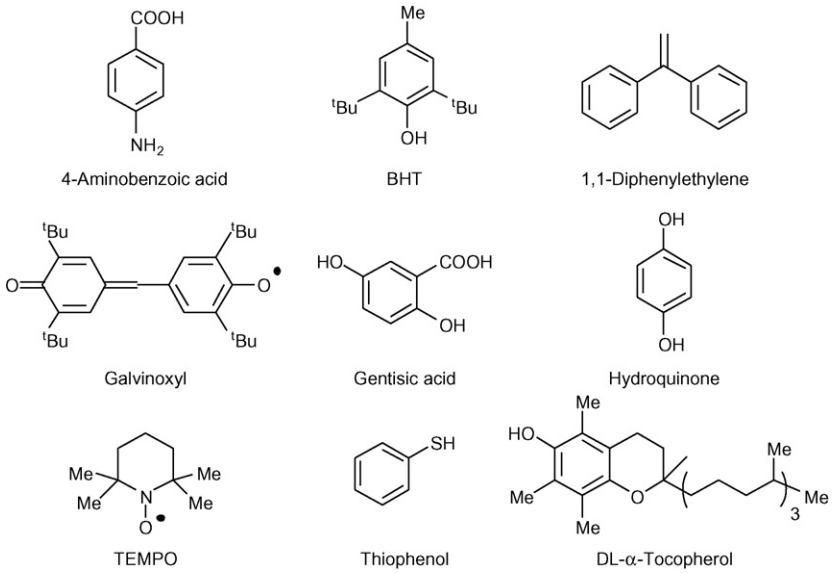


Fig. 2. Radical scavengers.

[34–36], hydroquinone [37–39], TEMPO [33,40], thiophenol [41], and DL-α-tocopherol [29].

The results in Table 2 demonstrate that the material yields of fluoroarene products, obtained by the fluoridation of iodonium salt **5**, are substainially increased by the addition of a radical scavenger, it is not expected that this particular improvement will influence the radiochemical yield of the process. The average yields are greatest for 1,1-diphenylethylene, TEMPO and galvinoxyl; however as the goal of this work was to improve the reproducibility of the process, the narrow range of results obtained in the presence of TEMPO highlighted this as the radical scavenger of choice.

Further studies were then undertaken to further optimise the reaction conditions to provide a standard robust protocol for the fluoridation of diaryliodonium salts. Such a protocol was essential to allow identification of an appropriate protecting group array necessary for the successful formation of polyfunctionalised fluorine-18 labelled radiopharmaceuticals.

Table 3 demonstrates that increasing the quantities of TEMPO does increase the yield slightly however the use of 10 mol% provides a more desirable profile (the most consistent results) and the protocol was therefore standardised at this level.

Table 3
Variation of the quantity of TEMPO

TEMPO (mol%)	Yield range[a,b] (%)	Average yield[c] (%)	**6**:**7**
0[d]	<5	n/a	1.2:1
1	19–23	20	1.3:1
5	22–29	26	1.3:1
10[e]	24–26	25	1.3:1
20	27–35	30	1.3:1
50	24–34	27	1.3:1
100	18–31	26	1.3:1
200	[f]	21	1.3:1

[a] CsF (2 equiv.), DMF, 90 °C, 1.5 h.
[b] By ^{19}F NMR relative to the internal standard 3-trifluoromethylanisole.
[c] Average of three runs.
[d] This work Table 1, entry 3.
[e] This work Table 2, entry 7.
[f] All three runs gave a yield of 21%.

The next parameters examined were temperature and the time of reaction (Tables 4 and 5). The effect of temperture appears quite pronounced with no reaction evident below 50 °C and only limited product formation at 70 °C suggesting an initiation temperature somewhere between the two. Increasing the temperature beyond this point rapidly improved the yield with 130 °C maintaining the required degree of reproducibility.

Under the conditions (DMF, 90 °C) used to establish the effect of time on the fluoridation of **5** it was evident that the yield of fluoroarenes rose over the first hour and then stabilised with additional time resulting in very little increase in yield. The observed decreases at extended reaction times are attributed to the degradation of the components of the reaction mixture.

A range of fluoride sources is used for the introduction of fluorine-18 and their effect was also examined (Table 6). The most common source—potassium fluoride, with a solubilising additive, still provided workable material yields of the fluoroarenes under the reaction conditions investigated.

Table 7 is a repeat of the initial reactions presented in Table 1 except that TEMPO (10 mol%) was now present. It is

Table 4
The effect of temperature on the fluoridation of **5**

T (°C)	Yield range[a,b] (%)	Average yield[c] (%)	**6**:**7**
50	n/a	0	n/a
70	6–12	9	1.3:1
90[d]	24–26	25	1.3:1
110	24–28	26	1.3:1
130	29–31	30	1.3:1
150	26–34	29	1.3:1

[a] CsF (2 equiv.), DMF, 1.5 h, TEMPO (10 mol%).
[b] By ^{19}F NMR relative to the internal standard 3-trifluoromethylanisole.
[c] Average of three runs.
[d] This work Table 2, entry 7.

Table 5
The effect of time on the fluoridation of **5**

Time (min)	Yield range[a,b] (%)	Average yield[c] (%)	**6**:**7**
15	–	<5	n/a
30	10–13	12	1.3:1
45	14–17	15	1.3:1
60	20–25	22	1.3:1
90[d]	20–24	25	1.3:1
120	19–24	21	1.3:1
24 h	21–28	23	1.3:1

[a] CsF (2 equiv.), DMF, 90 °C, TEMPO (10 mol%).
[b] By ^{19}F NMR relative to the internal standard 3-trifluoromethylanisole.
[c] Average of three runs.
[d] This work Table 2, entry 7.

Table 6
The effect of fluoridating agent

Fluoride source	Yield range[a,b] (%)	Average yield[c] (%)	**6**:**7**
CsF[d]	24–26	25	1.3:1
TBAF	<5	n/a	n/a
KF	<5	n/a	n/a
KF/K222[e]	8–10	9	1.3:1
KF/18C6[f]	12–15	13	1.3:1

[a] Fluoride source (2 equiv.), DMF, 90 °C, TEMPO (10 mol%), 1.5 h.
[b] By ^{19}F NMR relative to the internal standard 3-trifluoromethylanisole.
[c] Average of three runs.
[d] This work Table 2, entry 7.
[e] Kryptofix® 222: 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane.
[f] 18-Crown-6.

Table 7
Fluoridation of iodonium salt **5** in the presence of TEMPO (10 mol%)

Solvent[a]	Yield[b] (%)	**6**:**7**
MeCN	15	1.1:1
Me_2SO	25	1.3:1
DMF[c]	25	1.3:1
DMAC	17	1.4:1

[a] CsF (2 equiv.), 90 °C, TEMPO (10 mol%), 1.5 h.
[b] By ^{19}F NMR relative to the internal standard $PhCF_3$.
[c] This work Table 2, entry 7.

evident that the addition of the radical scavenger significantly improves the material yield of the fluoridation process and that the more polar aprotic solvents are preferred as the reaction medium.

3. Conclusion

In summary, the addition of a radical scavenger such as TEMPO, significantly improves the reproducibility of the process allowing the procedure to be used routinely for the first time. On a more general note the addition of radical scavengers also dramatically improves the material yield of fluoroarenes from the fluoridation of diaryliodonium salts yet does not appear to affect the selectivity of the process. The effect of these key modifications to the experimental procedure on the formation of fluorine-18 labelled aromatics will be reported elsewhere.

4. Experimental

Reactions requiring anhydrous conditions were performed using oven-dried glassware and conducted under a positive pressure of dinitrogen. Fluoride sources were purchased as anhydrous and used as supplied. Anhydrous solvents were prepared in accordance with standard protocols, or alternatively purchased from Aldrich in Sure/Seal™ bottles. IR spectra were recorded (4000–600 cm^{-1}) on a Perkin-Elmer Spectrum RX FT-IR Spectrometer with internal calibration. ^{1}H and ^{13}C NMR spectra were recorded on a Jeol GSX 270 spectrometer with residual protic solvent as an internal reference. ^{19}F NMR were recorded on a Jeol λ 500 MHz spectrometer with $CFCl_3$ as an external reference. Analysis of the crude reaction mixtures was achieved directly by ^{19}F NMR to focus on the desired products of the reaction and to more closely reflect the conditions employed when using fluorine-18. As a result the isolation of individual products was not pursued in this study. Elemental analyses were carried out at London Metropolitan University and are reported as the average of two runs. Mass spectra and accurate masses were recorded under CI^+ or FAB (+ve) conditions on a Micromass Platform II or a Micromass AUTOSPEC-Q instrument or at the EPSRC Mass Spectrometry Service. Melting points were recorded on a Reichert Microscope Hotstage Apparatus and are uncorrected.

4.1. Diacetoxyiodo-2-methoxybenzene (*4*)

Sodium perborate tetrahydrate (30.77 g, 200 mmol) was added portionwise to a solution of the 2-iodoanisole **3** (4.68 g, 20 mmol) in acetic acid (200 mL) at 45 °C. The mixture was stirred at this temperature for 4 h when water (500 mL) was added. The mixture was extracted with chloroform (3× 200 mL) and the organic layer concentrated *in vacuo* to give the crude product. Crystallisation gave **4** as a white crystalline solid (4.74 g, 13.46 mmol, 67%); mp 117–119 °C (from acetone–hexane) (lit., [42] 146.9–150.1 °C); Anal. Calcd. for $C_{11}H_{13}IO_5$: C, 37.5; H, 3.7. Found: C, 37.5; H, 3.8. IR (neat); ν 2937, 1618, 1582, 1475, 1365, 1275, 1251; δ_H (270 MHz; $CDCl_3$) 8.10 (1H, d, H6 *J* 8 Hz), 7.56 (1H, t, H5 *J* 8 Hz), 7.13 (1H, d, H3 *J* 8 Hz), 7.00 (1H, t, H4 *J* 8 Hz), 3.95 (3H, s, OCH_3), 1.93 (6H, s, $(OCOCH_3)_2$); δ_C (68 MHz; $CDCl_3$) 176.7 (CO), 156.3 (C3), 137.8, 134.6, 122.9, 113.4 (C1), 112.1, 57.0 (OMe), 20.5 ($(OCOMe)_2$); *m/z* (CI) 310 ($M + NH_3$, 23%), 293(M^+, 75), 234(75), 233(32), 109(36), 92(47), 91(56), 52(100). [Found: M^+, 292.9673. $C_9H_{10}IO_3$ requires 292.9675].

4.2. 4-Methoxy-2-methylphenyl(2-methoxyphenyl)iodonium trifluoroacetate (*5*)

Trifluoroacetic acid (0.77 mL, 10 mmol) was added dropwise, at −30 °C, to a stirred suspension of **4** (1.76 g, 5 mmol) in dichloromethane (50 mL). After 30 min the mixture was allowed to warm to room temperature and stirred for a further hour when it was recooled (−30 °C) and 3-methylanisole (611 mg, 5 mmol) was added. The resulting mixture was allowed to warm to room temperature overnight when the

solvent was removed *in vacuo* to give the crude product. Crystallisation gave **5** as a white crystalline solid (2.17 g, 4.63 mmol, 93%); mp 144–146 °C (from dichloromethane–hexane); Anal. Calcd. for $C_{17}H_{16}IO_4F_3$: C, 43.6; H, 3.4. Found C, 43.6; H, 3.5. IR (KBr): ν 3082, 2839, 1656, 1564, 1440, 1286, 1174; δ_H (270 MHz; d_6-Me_2SO) 8.28 (1H, d, H6′ *J* 8 Hz), 8.17 (1H, d, H6 *J* 9 Hz), 7.62 (1H, t, H4′ *J* 8 Hz), 7.27 (1H, d, H3′ *J* 8 Hz), 7.07 (2H, m, H3/H5′), 6.83 (1H, dd, H5 *J* 3, 9 Hz), 3.93 (3H, s, 2′-OMe), 3.77 (3H, s, 4-OMe), 2.60 (3H, s, 2-C*H*$_3$); δ_C (68 MHz; d_6-Me_2SO) 162.7, 156.8, 143.4, 139.4 (C6), 137.6 (C6′), 135.0 (C4′), 123.8 (C5′), 117.2 (C3), 115.2 (C5), 113.4 (C3′), 110.7, 107.4, 57.4 (2′-OMe), 56.1 (4-OMe), 25.4 (Me); *m/z* (FAB) 356($M+H^+$, 16%), 355(M^+, 100). [Found: M^+, 355.0192. $C_{15}H_{16}IO_2$ requires 355.0195].

4.3. Fluoridation procedure: Tables 1 and 7

Iodonium salt **5** (0.022 g, 0.05 mmol) in the appropriate solvent (1 mL), caesium fluoride (0.015 g, 0.1 mmol) in the same solvent (1.5 mL) and finally TEMPO (10 mol%) as a solution in MeCN (0.1 mL) if required (Table 7) were added to a carousel tube [43] (predried at 140 °C, evacuated and flushed with nitrogen). The carousel tube was then placed on a carousel reactor preheated to 90 °C and heated under nitrogen for 1.5 h. After this time the tubes were removed from the reactor, cooled to room temperature rapidly and analysed by ^{19}F NMR. The yield was calculated using benzotrifluoride as an internal standard.

4.4. Fluoridation procedure: Tables 2, 3 and 6

The fluoride source (0.1 mmol), radical scavenger solution (appropriate mol% in MeCN, 0.1 mL) and iodonium salt **5** (0.022 g, 0.05 mmol) in DMF (2.5 mL) were added to a carousel tube [43] (predried at 140 °C, evacuated and flushed with nitrogen). The carousel tube was then placed on a carousel reactor preheated to 90 °C and heated for 1.5 h. After this time the tubes were removed from the reactor, cooled to room temperature rapidly and analysed by ^{19}F NMR. The yield was calculated using 3-trifluoromethylanisole as an internal standard.

4.5. Fluoridation procedure: Table 4

Caesium fluoride (0.015 g, 0.1 mmol), TEMPO (10 mol%) as a solution in MeCN (0.1 mL) and iodonium salt **5** (0.022 g, 0.05 mmol) in DMF (2.5 mL) were added to a carousel tube [43] (predried at 140 °C, evacuated and flushed with nitrogen). The carousel tube was then placed on a carousel reactor preheated to the relevant temperature and heated for 1.5 h. After this time the tubes were removed from the reactor, cooled to room temperature rapidly and analysed by ^{19}F NMR. The yield was calculated using 3-trifluoromethylanisole as an internal standard.

4.6. Fluoridation procedure: Table 5

Caesium fluoride (0.015 g, 0.1 mmol), TEMPO (10 mol%) as a solution in MeCN (0.1 mL) and iodonium salt **5** (0.022 g, 0.05 mmol) in DMF (2.5 mL) were added to a carousel tube [43] (predried at 140 °C, evacuated and flushed with nitrogen). The carousel tube was then placed on a carousel reactor preheated to 90 °C and heated for the required time. At the time intervals stated in Table 5 aliquots (0.3 mL) were taken, cooled to room temperature rapidly, diluted with DMF (0.4 mL) and analysed by ^{19}F NMR. The yield was calculated using 3-trifluoromethylanisole as an internal standard.

Acknowledgement

We thank GE-Healthcare for funding and the EPSRC for provision of the Swansea Mass Spectrometry Service.

References

[1] P.J. Stang, V.V. Zhdankin, Chem. Rev. 96 (1996) 1123–1178.
[2] A. Varvoglis, Hypervalent Iodine in Organic Synthesis, Academic Press, London, 1997.
[3] A. Varvoglis, S. Spyroudis, Synlett (1998) 221–232.
[4] T. Wirth, U.H. Hirt, Synthesis (1999) 1271–1287.
[5] T. Wirth, Top. Curr. Chem. 224 (2003).
[6] M. van der Puy, J. Fluorine Chem. 21 (1982) 385–392.
[7] S. Martín-Santamaría, M.A. Carroll, C.M. Carroll, C.D. Carter, V.W. Pike, H.S. Rzepa, D.A. Widdowson, Chem. Commun. (2000) 649–650.
[8] M.A. Carroll, L.M. Kamara, D.A. Widdowson, V.W. Pike, J. Labelled Compd. Radiopharm. 48 (2005) 519–520.
[9] M. Guillaume, A. Luxen, B. Nebeling, M. Argentini, J.C. Clark, V.W. Pike, Appl. Radiat. Isot. 42 (1991) 749–762.
[10] A. Shah, D.A. Widdowson, V.W. Pike, J. Labelled Compd. Radiopharm. 39 (1997) 65–67.
[11] A. Shah, V.W. Pike, D.A. Widdowson, J. Chem. Soc., Perkin Trans. 1 (1998) 2043–2045.
[12] F.R. Wüst, T. Kniess, J. Labelled Compd. Radiopharm. 46 (2003) 699–713.
[13] F.R. Wüst, A. Hohne, P. Metz, Org. Biomol. Chem. 3 (2005) 503–507.
[14] F. Wüst, J.M.H.M. Reul, T. Rein, A. Abel, G. Stöcklin, J. Labelled Compd. Radiopharm. 44 (2001) S12–S14.
[15] V.W. Pike, F.I. Aigbirhio, J. Chem. Soc., Chem. Commun. (1995) 2215–2216.
[16] J. Ermert, C. Hocke, T. Ludwig, R. Gail, H.H. Coenen, J. Labelled Compd. Radiopharm. 47 (2004) 429–441.
[17] S. Freeman, J.F. Alder, Eur. J. Med. Chem. 37 (2002) 527–539.
[18] A. Luxen, M. Guillaume, W.P. Melega, V.W. Pike, O. Solin, R. Wagner, Nucl. Med. Biol. 19 (1992) 149–158.
[19] E.S. Garnett, G. Firnau, C. Nahmias, Nature 305 (1983) 137–138.
[20] H.F. VanBrocklin, M. Blagoev, A. Hoepping, J.P. O'Neil, M. Klose, P.A. Schubiger, S. Ametamey, Appl. Radiat. Isot. 61 (2004) 1289–1294.
[21] M.A. Carroll, S. Martín-Santamaría, V.W. Pike, H.S. Rzepa, D.A. Widdowson, J. Chem. Soc., Perkin Trans. 2 (1999) 2707–2714.
[22] V.V. Grushin, Acc. Chem. Res. 25 (1992) 529–536.
[23] V.V. Grushin, I.I. Demkina, T.P. Tolstaya, J. Chem. Soc., Perkin Trans. 2 (1992) 505–511.
[24] M.A. Carroll, unpublished results.
[25] A. McKillop, D. Kemp, Tetrahedron Lett. 45 (1989) 3299–3306.
[26] M.A. Carroll, V.W. Pike, D.A. Widdowson, Tetrahedron Lett. 41 (2000) 5393–5396.
[27] M.-L. Hu, Y.-K. Chen, L.-C. Chen, M. Sano, Nutr. Biochem. 6 (1995) 504–508.
[28] G.M. Williams, M.J. Iatropoulos, J. Whysner, Food Chem. Tox. 37 (1999) 1027–1038.
[29] E. Mendis, N. Rajapakse, S.-E. Kim, J. Agric. Food Chem. 53 (2005) 581–587.
[30] D.J. McPhee, M. Campredon, M. Lesage, D. Griller, J. Am. Chem. Soc. 111 (1989) 7563–7567.

[31] M. Yamada, K. Kato, M. Nomizu, N. Sakairi, K. Ohkawa, H. Yamamoto, N. Nishi, Chem. Eur. J. 8 (2002) 1407–1412.
[32] M. Ochiai, A. Nakanishi, T. Ito, J. Org. Chem. 62 (1997) 4253–4259.
[33] M. Ochiai, T. Ito, H. Takahashi, A. Nakanishi, M. Toyonari, T. Sueda, S. Goto, M. Shiro, J. Am. Chem. Soc. 118 (1996) 7716–7730.
[34] K. Ashidate, M. Kawamura, D. Mimura, H. Tohda, S. Miyazaki, T. Teramoto, Y. Yamamoto, Y. Hirata, Eur. J. Pharm. 513 (2005) 173–179.
[35] M. Hermann, S. Kapiotis, R. Hofbauer, C. Seelos, I. Held, B. Gmeiner, Free Radic. Biol. Med. 26 (1999) 1253–1260.
[36] S. Liu, D.S. Edwards, Bioconjugate Chem. 12 (2001) 554–558.
[37] J.R. Anderson, W.R. Jackson, Z. Yang, E.M. Campi, Catal. Lett. 45 (1997) 197–201.
[38] S.H. Jhung, J.-H. Lee, A.K. Cheetham, G. Ferey, J.-S. Chang, J. Catal. 239 (2006) 97–104.
[39] T.-Y. Lu, C. Xue, F.-T. Luo, Tetrahedron Lett. 44 (2003) 1587–1590.
[40] E. Damiani, P. Astolfi, L. Cionna, F. Ippoliti, L. Greci, Free Radic. Res. 40 (2006) 485–494.
[41] G.W. Sluggett, C. Turro, M.W. George, I.V. Koptyug, N.J. Turro, J. Am. Chem. Soc. 117 (1995) 5148–5153.
[42] J.E. Leffler, L.J. Story, J. Am. Chem. Soc. 89 (1967) 2333–2338.
[43] Radleys Carousel 12 Reaction Station. http://www.radleys.com.