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OAK RIDGE NATIONAL LABORATORY

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NUCLEAR MEDICINE PROGRAM PROGRESS REPORT FOR QUARTER ENDING March 31, 1996

F. F. Knapp, Jr.

K. R. Ambrose
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F. Mokler

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ORNL/TM-6771
ORNL/TM-6916
ORNL/TM-6958
ORNL/TM-7072
ORNL/TM-7223
ORNL/TM-7411
ORNL/TM-7482
ORNL/TM-7605
ORNL/TM-7685
ORNL/TM-7775
ORNL/TM-7918
ORNL/TM-8123
ORNL/TM-8186
ORNL/TM-8363
ORNL/TM-8428
ORNL/TM-8533
ORNL/TM-8619
ORNL/TM-8746
ORNL/TM-8827
ORNL/TM-8966
ORNL/TM-9037
ORNL/TM-9124
ORNL/TM-9343
ORNL/TM-9394
ORNL/TM-9480
ORNL/TM-9609
ORNL/TM-9707
ORNL/TM-9784
ORNL/TM-9937
ORNL/TM-10082
ORNL/TM-10238
ORNL/TM-10294
ORNL/TM-10377
ORNL/TM-10441
ORNL/TM-10618
ORNL/TM-10711
ORNL/TM-10839
ORNL/TM-11014
ORNL/TM-11043
ORNL/TM-11145
ORNL/TM-11224
ORNL/TM-11304
ORNL/TM-11377
ORNL/TM-11427
ORNL/TM-11550
ORNL/TM-11570
ORNL/TM-11721
ORNL/TM-11755
ORNL/TM-11830
ORNL/TM-11881
ORNL/TM-11992
ORNL/TM-12054
ORNL/TM-12110
ORNL/TM-12159
ORNL/TM-12222
ORNL/TM-12312
ORNL/TM-12343
ORNL/TM-12411
ORNL/TM-12485
ORNL/TM-12661
ORNL/TM-12707
ORNL/TM-12789
ORNL/TM-12875
ORNL/TM-12909
ORNL/TM-12965
ORNL/TM-13053
ORNL/TM-13107
ORNL/TM-13150

CONTENTS

SUMMARY

Biodistribution studies with the radioiodinated 3(R)- and 3(S)-BMIPP isomers in rats have shown that 3(R)-BMIPP has 20-25% higher heart uptake (15-180 min) than 3(S)-BMIPP, while uptake in other tissues examined is similar. To evaluate the possible differences in metabolic fate of the two isomers, a mixture of [I-125]-3(R)/[I-131]-3(S)-BMIPP was administered to fasted female Fisher rats. Groups (n = 3 rats per group) were sacrificed after 15, 60 and 180 min, and urine and feces collected from another group. Samples of blood, heart, liver, lungs, kidney, and urine were Folch-extracted. The distribution of I-125 and I-131 in the organic, aqueous, and pellet samples were determined. Organic samples were then analyzed by thin-layer chromatography (TLC) and high performance liquid chromatography (HPLC). The relative distribution of I-125/I-131 in the lipid, aqueous, and pellet samples was similar for both isomers. Distribution of I-125/I-131 in the various components of the lipid extracts observed by TLC was also similar, with principal incorporation into the free fatty acid (FFA) and triglyceride (TG) pools. HPLC analyses (C18) of the FFA fraction showed similar I-125/I-131 profiles, corresponding to BMIPP, and the α-methyl-C_{14} (PIPA) and C_{12}, C_{10} and C_6 carbon chain-length catabolites. By TLC, urine I-125/I-131 chromatographed with hippuric acid. HPLC analyses (C18) of acid-hydrolyzed urine gave a single I-125/I-131 component with the same RRT as 2-(p-iodophenyl)acetic acid, the final α/β-oxidative BMIPP catabolite. Unexpectedly, HPLC of lipids from base hydrolyzed TG from the heart tissue, showed I-125/I-125 co-chromatographing with short-chain fatty acids, with only levels in BMIPP. These unexpected results demonstrate that the 3(R)-BMIPP and 3(S)-BMIPP isomers are metabolized similarly in rat tissues, and that the higher myocardial extraction observed for the 3(R)-BMIPP may reflect differences in the relative membrane transport of the two isomers.

A facile stereoselective synthesis of α-hydroxy-α-(1-propyn-3-yl)-α-phenylacetic acid in high enantiomeric excess has been developed and allows determination of the (R/S) conformation at this center. By comparison of the specific rotation, HPLC, and NMR data of E-R,R- and E-R,S-IQNP to those prepared by the classical resolution of the acetate moiety allows the assignment of E-R,R-IQNP as the isomer demonstrating binding to the M_1 mAChR subtype and Z-R,R-IQNP as the isomer binding to both the M_1 and M_2 mAChR subtypes.

Also during this period several radioisotopes generators and other medical radioisotopes were provided to collaborators for joint research, including tungsten-188/rhenium-188 generators which were provided to Columbia University, New York, University of Alabama Medical School in Birmingham, Alabama, and the Beijing Normal University, in Beijing, China. In addition, tungsten-188 sodium tungstate solution was provided to the Nuclear Research Center in Shanghai, China, for fabrication of tungsten-188/rhenium-188 generators for research projects for rhenium-188-labeling of therapeutic agents.

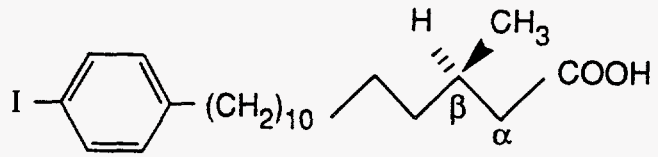
Medical radioisotopes which were provided for full cost recovery through the ORNL Isotope Production and Distribution Program included samples of high specific activity rhenium-186 which were provided to prospective customers to assess the radiolabeling efficiency of this radioisotope produced in the ORNL HFIR. Organizations included Mallinckrodt Medical, in Petten, Holland, Mallinckrodt Medical, in St. Louis, Missouri, and NeoRx, Inc., in Seattle, Washington. In addition, tungsten-188/rhenium-188 generators were sold to Austin Hosptial in Melbourne, and ANSTO in Sydney, Australia.

Resolution and Evaluation in Rat Tissues of the Metabolism of Radioiodinated 3(R)- and 3(S)-Isomers of 15-(p-iodophenyl)-3-methylpentadecanoic Acid ("BMIPP")

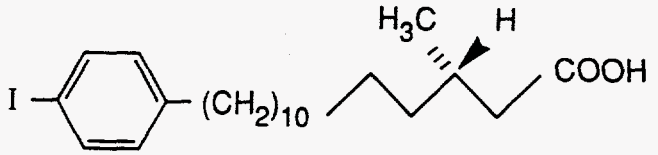
Clinical SPECT comparison of regional myocardial distribution of the racemic [I-123]-3-(R,S)-BMIPP fatty acid analogue (Figure 1) with flow tracers (Sestamibi, Tl-210) is an important method for identifying post-ischemic viable myocardium.[1-4] The strategy for our development of BMIPP was the expectation that introduction of the 3-methyl group would inhibit oxidative metabolism by the usual β-oxidative pathway.[5] In this manner, minimal regional redistribution would occur during the time period required for data acquisition for SPECT. Initial planar imaging studies in humans demonstrated the prolonged myocardial retention of [I-123]-BMIPP in comparison with the [I-123]-IPPA straight-chain analogue.[6] Using this unique "metabolic trapping" mechanism, high quality SPECT images are obtained which represent the original "frozen" regional uptake pattern.[8-11]

We have recently reported the first resolution[11], radioiodination and tissue distribution studies *in rats*[12-13] with the 3(R)- and 3(S)-isomers of BMIPP, which showed higher myocardial uptake of the 3(R)-BMIPP isomer in comparison with 3(S)-BMIPP (ORNL/TM-13150). Although uptake of 3(R)-BMIPP is higher (20-25%), the relative myocardial washout curves for both isomers have similar shapes, while uptake and washout of most other tissues, including blood, lung, liver and kidney, is similar. In order to more carefully evaluate the relative metabolism of each isomer, the present studies were focussed on a detailed evaluation of the relative uptake and flux of 3(R)-BMIPP and 3(S)-BMIPP through the various lipid pools. By administration of a dual-labeled [I-125]-3(R)-BMIPP/[I-131]-3(S)-BMIPP mixture to rats, each rat essentially served as its own control.

The distribution of iodine-125 [from (3R)-BMIPP] and iodine-131 [from 3(S)-BMIPP] (Table 1) was similar to the results of similar experiments reported earlier (ORNL/TM-13150), in which there was higher myocardial uptake of 3(R)-BMIPP compared to the 3(S)-BMIPP isomer.[11-13] The results of the Folch extraction studies (Table 2) show essentially no differences in the distribution of [I-125]-3(R)-BMIPP and [I-131]-3(S)-BMIPP in the organic, aqueous, and pellet fractions and were similar to data reported earlier for the metabolism of racemic BMIPP in rats *in vivo*[14-15] and Langendorff-perfused rat hearts.[13-17]



3 (R) - BMIPP



3 (S) - BMIPP

Figure 1. Structure of 3(R)-BMIPP and 3(S)-BMIPP

Table 1. Distribution of Radioactivity in Tissues of Groups of Fasted Female Fisher Rats Following Intravenous Administration of a Dual-Labeled Mixture of [I-125]-3(R)-BMIPP and [I-131]-3(S)-BMIPP

Per Cent Injected Dose Per Gram of Tissue Values ± S.D.						
Minutes After Injection	BMIPP Isomer	Blood	Heart	Liver	Lungs	Thyroid
15	[I-125]-3(R)-	2.20 ± 0.31	**5.02** ± 0.21	2.79 ± 0.28	1.33 ± 0.29	17.16 ± 6.8
	[I-131]-3(S)-	2.13 ± 0.30	**4.34** ± 0.34	3.93 ± 0.46	1.98 ± 0.10	15.58 ± 6.4
60	[I-125]-3(R)-	1.74 ± 0.12	**3.17** ± 0.43	1.91 ± 0.18	1.29 ± 0.08	15.15 ± 7.6
	[I-131]-3(S)-	1.74 ± 0.11	**2.32** ± 0.23	2.29 ± 0.26	1.53 ± 0.12	14.10 ± 7.2
180	[I-125]-3(R)-	1.60 ± 0.08	**2.32** ± 0.69	1.22 ± 0.19	1.08 ± 0.05	10.26 ± 4.1
	[I-131]-3(S)-	1.61 ± 0.11	**1.72** ± 0.45	1.10 ± 0.20	1.36 ± 0.13	8.53 ± 3.4

- Three fasted rats were studied for each group. Each rat was injected via a lateral tail vein with a mixture of 12 μCi [I-125]-3(R)-BMIPP and 30 μCi [I-131]-(3S)-BMIPP complexed to a 6% BSA solution.

Radioactivity migrating in the region of the free fatty acids by TLC in our earlier studies was identified as unmetabolized BMIPP.[14-15] More recently, however, catabolism of BMIPP by a process involving initial α-oxidation preceding subsequent β-oxidation has been experimentally confirmed.[17] The metabolite 14-(p-iodophenyl)-α-methyltetradecanoic acid (AMIPT) has been isolated and identified, as originally had been suggested.[1-4,14] The availability of the authentic 14-(p-iodophenyl)-α-(R,S)-methyltetradecanoic acid analogue (AMIPT; kindly provided by Dr. Y. Yamamichi, *et al.*, Central Research Laboratory, Nihon Medi-Physics, Ltd.,Chiba, Japan) provided an opportunity in the present studies to compare the TLC and HPLC mobility of the radioiodinated metabolites formed from 3(S)-BMIPP and 3(R)-BMIPP. By comparison of the relative mobility of the radioactive metabolites with authentic AMIPT, results from the present HPLC study confirm that the radioactive catabolites from both [I-125]-3(R)-BMIPP and [I-131]-3(S)-BMIPP correspond to the fourteen carbon chain-length AMIPT metabolite (Figure 2). In addition to the evaluation of the identity of components of the free fatty acid pool in tissue extracts following intravenous administration of the radioactive dual-labeled 3(S)/3(R)-BMIPP mixture, we also evaluated the acidic components obtained by saponification of the triglyceride fraction obtained by column chromatography of the myocardial lipid extracts. The non-saponifiable fraction was analyzed by both TLC and HPLC analyses. While TLC demonstrated the presence of components more polar than BMIPP and AMIPT which suggested short chain acidic metabolites, HPLC analysis (Figure 2) confirmed that the acidic fraction released by basic hydrolysis appears to consist primarily of short chain rather than BMIPP as was initially presumed[1-4]. In the earlier studies, only the triglyceride fraction was isolated and not hydrolyzed.

Table 2. Mean PerCent Distribution of I-125 and I-131 In Organic, Aqueous and Pellet Fractions From Folch-Extracted Rat Tissues Following Intravenous Administration of a Mixture of [I-125]-3(R)-BMIPP and [I-131]-3(S)-BMIPP.

Per Cent Injected Dose per Gram of Tissue ± S.D.						
	Organic Phase		Aqueous		Pellet	
Tissue/Sample	I-125	I-131	I-125	I-131	I-125	I-131
Heart 15	79.5 ± 2.90	79.6 ± 5.12	4.98 ± 0.76	5.87 ± 0.93	16.5 ± 2.61	14.5 ± 1.73
Heart 60	75.1 ± 14.1	75.7 ± 2.06	5.48 ± 1.39	7.68 ± 2.06	19.5 ± 6.50	17.1 ± 4.54
Heart 180	79.0 ± 18.6	80.0 ± 18.4	3.38 ± 1.56	4.45 ± 2.09	17.6 ± 5.73	15.5 ± 4.23
Blood 15	11.6 ± 0.94	12.1 ± 1.00	41.1 ± 0.61	40.6 ± 2.07	44.4 ± 30.7	43.7 ± 31.3
Blood 60	5.1 ± 1.97	5.5 ± 2.03	38.5 ± 3.33	40.2 ± 3.85	48.8 ± 21.4	47.7 ± 21.9
Blood 180			24.8 ± 7.57	26.5 ± 8.37	70.1 ± 8.34	68.0 ± 11.6
Liver 15	44.9 ± 7.01	45.9 ± 5.66	15.3 ± 3.02	15.3 ± 2.86	39.9 ± 8.10	38.8 ± 8.18
Liver 60	38.5 ± 6.57	38.7 ± 5.48	15.6 ± 1.15	15.6 ± 0.86	45.5 ± 7.21	45.7 ± 6.60
Liver 180	37.8 ± 10.9	37.8 ± 9.90	17.7 ± 1.26	17.7 ± 1.24	45.3 ± 12.9	44.4 ± 10.9
Lung 15	44.9 ± 5.68	48.8 ± 5.25	31.1 ± 4.31	30.2 ± 4.05	23.9 ± 5.21	21.1 ± 4.32
Lung 60	35.9 ± 3.08	37.4 ± 2.39	37.7 ± 5.13	37.4 ± 4.59	26.7 ± 4.96	25.2 ± 6.76
Lung 180	40.7 ± 9.21	37.3 ± 3.56	32.9 ± 5.85	35.0 ± 6.46	26.4 ± 9.72	27.7 ± 9.06
Kidney 15	29.2 ± 0.66	31.2 ± 0.71	42.5 ± 3.38	41.8 ± 4.59	28.3 ± 12.3	26.9 ± 11.9
Kidney 60	33.1 ± 0.91	32.4 ± 2.86	16.9 ± 1.68	18.8 ± 1.10	19.9 ± 1.04	18.9 ± 2.20
Kidney 180	24.2 ± 3.17	23.8 ±2.83	55.3 ± 5.31	56.1 ± 4.78	20.8 ± 2.4	20.1 ± 1.41

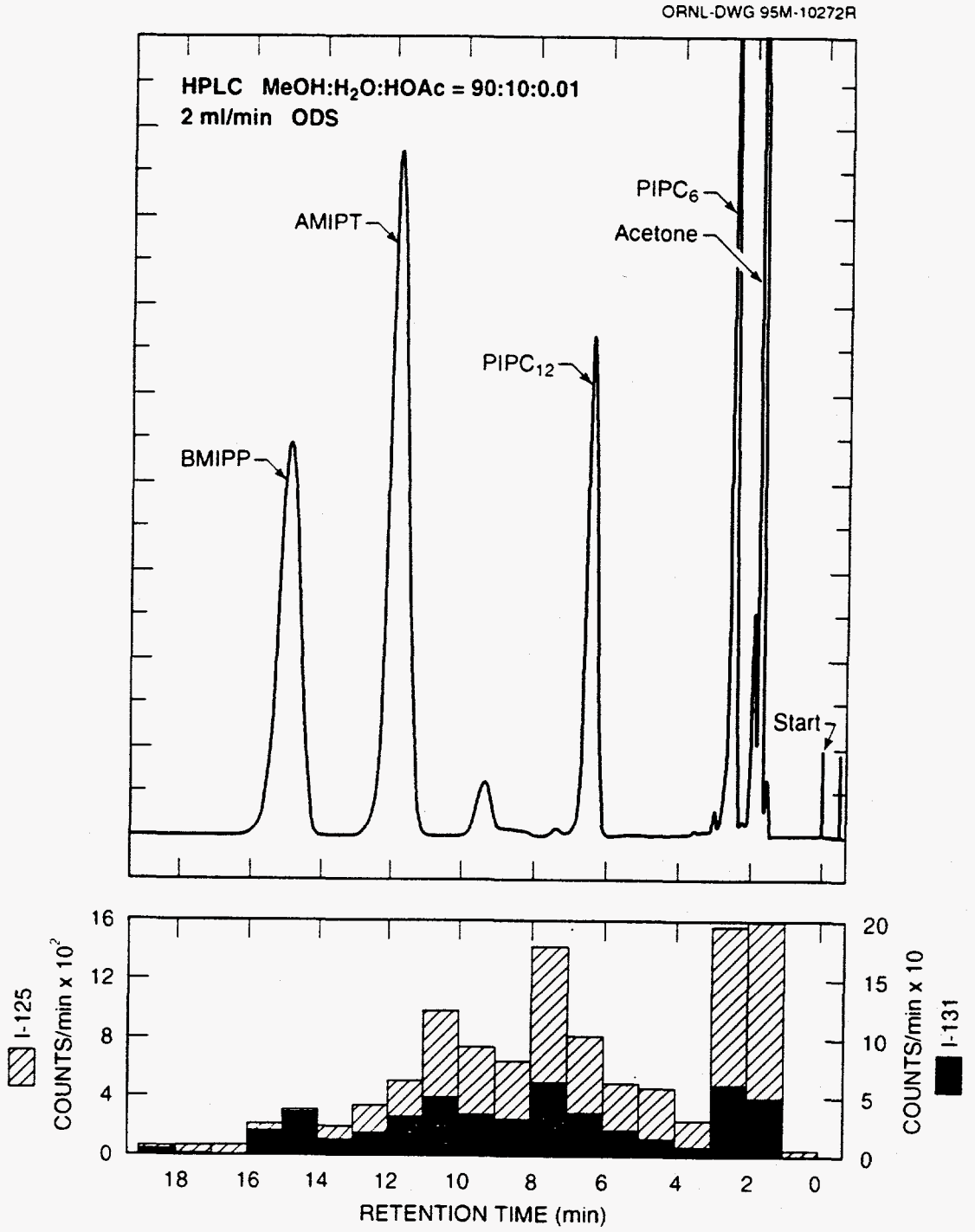


Figure 2. HPLC separation of the free fatty acid fraction obtained by basic hydrolysis of the pooled triglyceride fractions obtained by column chromatography of the pooled neutral lipids from the Folch extracted fraction from rat hearts obtained 30 min following intravenous adminsitration of a [I-125]-3(R)-BMIPP/[I-131]-3(S)-BMIPP mixture.

Urine and feces, collected over a one-week period, indicated rapid excretion of radioactivity with exactly the same profiles for iodine-125 and iodine-131. Most of the activity was excreted in the urine (Figure 3). The relative radioactivity excreted from 3(R)-BMIPP (iodine-125) and 3(S)-BMIPP (iodine-131) was very similar. Analysis of the radioactive components of the urine indicated the presence of a single component which co-chromatrographed with hippuric acid (Figure 5), demonstrating conjugation of the acidic metabolite(s) with endogenous amines, similar to hippuric acid. Samples of urine were combined with concentrated HCl and heated at 175°C in a Teflon vessel housed in a stainless steel bomb. After cooling, the dark-colored solution was extracted with chloroform and the organic layer washed with water and dried. Most of the radioactivity was found in the organic fraction and TLC analysis demonstrated the presence of a single component more polar than BMIPP and AMIPT. Analysis by HPLC demonstrated the presence of single iodine-125 and iodine-131 component which co-chromatographed with 2-[p-(iodophenyl)]acetic acid (Figure 4).

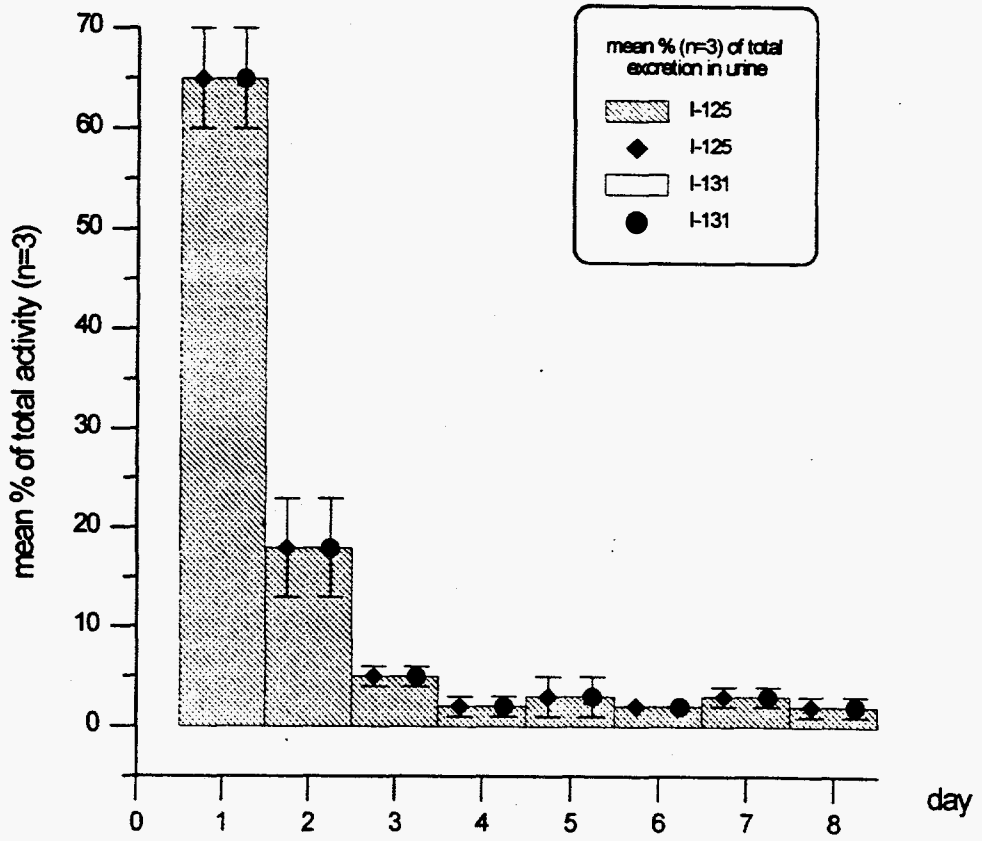


Figure 3. Excretion of radioiodinated metabolites in urine following administration of the [I-125]-3(R)-BMIPP/[I-131]-3(S)-BMIPP mixture.

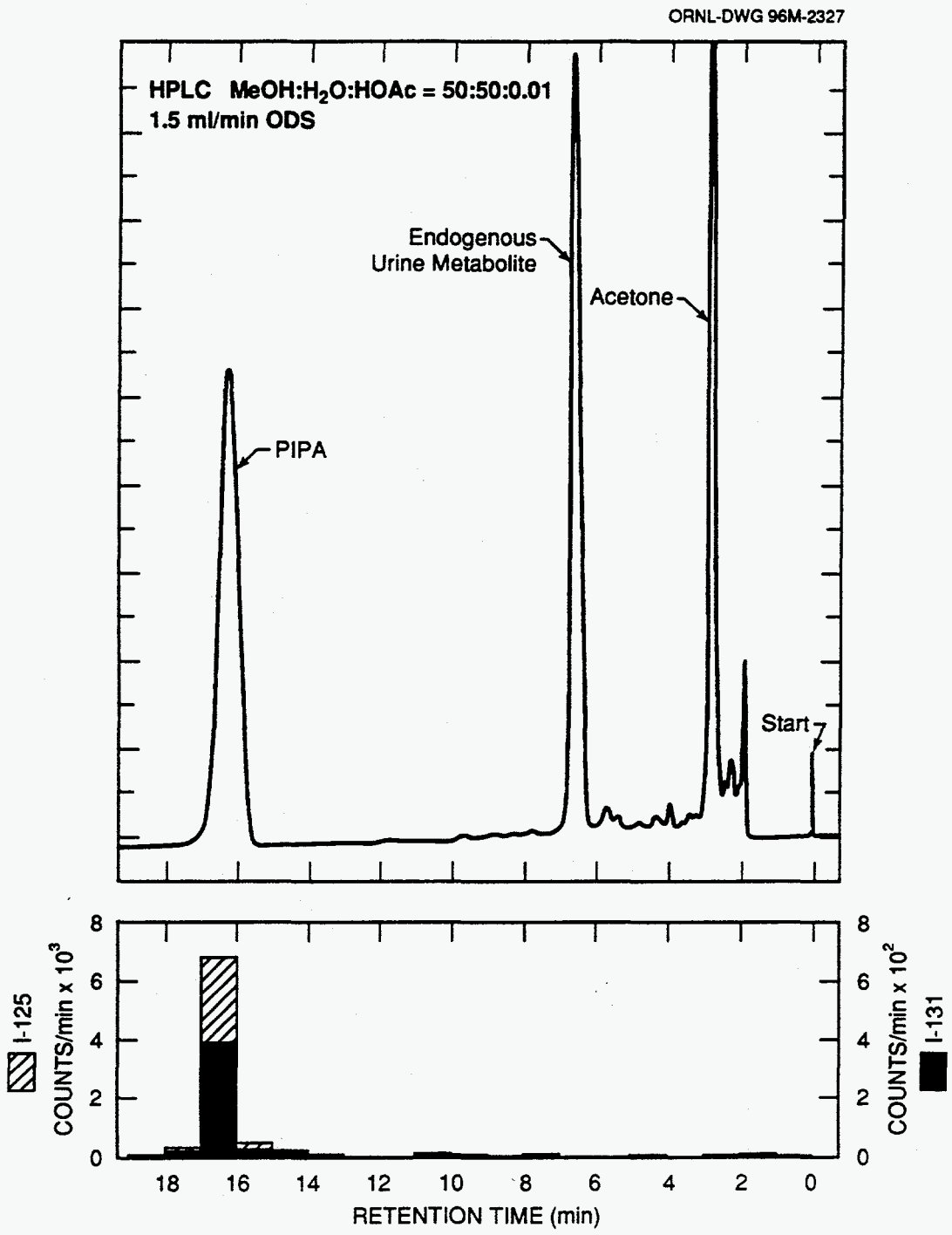


Figure 4. HPLC analysis of the neutral fraction obtained by acid hydrolysis of urine of rats following administration of the [I-125]-3(R)-BMIPP/[I-131]-3(S)-BMIPP mixture.

The availability of the 3(S)-BMIPP and 3(R)-BMIPP isomers and authentic samples of AMIPT and 2-[p-(iodophenyl)]acetic acid (PIPA) has provided an opportunity to dissect the relative metabolism of the two isomers for the first time. The major importance of our results is that we have shown that both isomers appear to be metabolized in the same manner. We were surprised that analysis of the free acids released by basic hydrolysis of the myocardial lipids demonstrated a mixture of fatty acids with chain lengths less that BMIPP. In addition, we have conclusively shown that radioactivity excreted in the urine consists exclusively of conjugates of 2-[(p-iodophenyl)]acetic acid. Although the relative myocardial uptake of the 3(R)-BMIPP is considerably greater than 3(S)-BMIPP, the present studies have shown that there appears to be no differences in the lipid pool distribution of the isomers observed in the 15-180 minute time frame studied. The reasons for the enhanced myocyte uptake of 3(R)-BMIPP observed in rats in comparison to 3(S)-BMIPP are unclear, but the difference may be expected to result from differences in the membrane translocation of the two isomers from the intravascular space into the myocytes. How significant this difference may be in relation to the clinical use of BMIPP remains to be seen. If a similar difference is observed in larger experimental animals, the clinical evaluation of the relative myocardial uptake of 3(R)-BMIPP and 3(S)-BMIPP may be justified. These results are important in expanding our understanding of the metabolism of BMIPP.

Structure Elucidation Via Stereoselective Synthesis of the Acetate Center of 1Azabicyclo[2.2.2]oct-3yl α-Hydroxy-α-(1-iodo-1-propen-3-yl) - α-phenylacetate (IQNP). A New Muscarinic Imaging Agent for SPECT

1-Azabicyclo[2.2.2]oct-3yl α-Hydroxy-α-(1-iodopropen-3-yl)-α-phenylacetate (IQNP,1) has been developed as a new imaging agent for use in Single Photon Emission Computed Tomography (SPECT) (ORNL/TM-12110, -11811 and -11992). IQNP has been shown to be readily radioiodinated, to cross the blood brain barrier and to localize in regions of the brain which contain varying concentrations of the muscarinic acetylcholine receptor complex (mAChr).[19] In addition, the various stereoisomers of IQNP demonstrate modest selectivity for the various subtypes of the mAChr.[20-21] The stereochemistry of 3-quinuclidinol is well established[23] and the R-(-) configuration of various 3-quinuclidinyl esters has been shown to impart mAChR binding activity to the ligands.[24-25] The acetate moiety of (**1**) has recently been resolved as the (-)- and (+)-α-methylbenzylamine salts.[20]

Biodistribution studies in rats have demonstrated that E- and Z-IQNP which contain the (-) configuration of the acetate moiety have significant uptake in areas of the brain rich in mAChR and the heart. However, **1** is isolated as an oil and the R/S orientation of the acetate moiety has yet to be identified due to the absence of a suitable crystal for analysis.

A stereoselective α-alkylation of α-heterosubstitiuted acids has been reported to afford diastereoselectivities of >95%[26,27]. The condensation of S-(+)-mandelic acid with trimethylacetaldehyde affords *cis*-(2S,5S)-2-(t-butyl)-5-phenly-1,3-dioxolan-4-one (**2**). It has been demonstrated that after deprotonation with base, the electrophilic reaction with alkyl halides occurs on the least hindered face with retention of configuraiton. The acetate moiety was then prepared via a stereoselective synthesis involving (2S,5S)- and (2R,5R)-**2** as shown in Figure 5. (2S,5S)-and (2R,2R)-2-(t-butyl)-5-phenly-1,3-dioxolan-4-one (**2**) were prepared from the condensation of trimethylacetaldehyde with S- or R-mandelic acid, respectively. A tetrahydrofuran solution of (2S,5S)-2-(t-butyl)-5-phenyl-1,3-dioxolan-4-one (2S,5S-**2**, 5.0 mmol) was slowly added to a solution of lithium hexamethyldisilizane (5.2 mmol) in tetrahydrofuran at -78°C and stirred for 15 minutes followed by the addition of propargyl bromide (11.2 mmol). The solution was warmed to room temperature and stirred for 3 hours to afford (2S,5S)-2-(t-butyl)-5-phenyl-5-(1-propyn-3-yl)-1,3-dioxolan-4-one (S,S-**3**) after purification by Kugelrohr distillation (100-110°C). Compound **3** was then treated with a 2M methanolic sodium hydroxide solution at 60°C for 20 minutes to afford S-(+)-α-hydroxy-α-phenyl-α-(1-propyn-3-yl) acetic acid (S-(+)-**4**).

Since it has been shown that the addition of the alkyl group occurs on the least hindered side of **2**, the alkylation of (2S,5S)-**2** with propargyl bromide affords (2S,5S)-**3**. Subsequent basic hydrolysis of (2S,5S)-**3** affords S-4. By the comparison of the specific rotation (Table 3) of α-hydroxy-α-phenyl-α-(1-propyn-3-yl)acetic acids obtained from the stereoselective route and that by the classical resolution, the isomer which reflects polarized light in the (+) direction can be assigned as S-**4** and the isomer which reflects light in the (-) direction as R-**4**. We have previously shown that the stereoisomers of the acetate center of IQNP can be separated using a normal phase column,

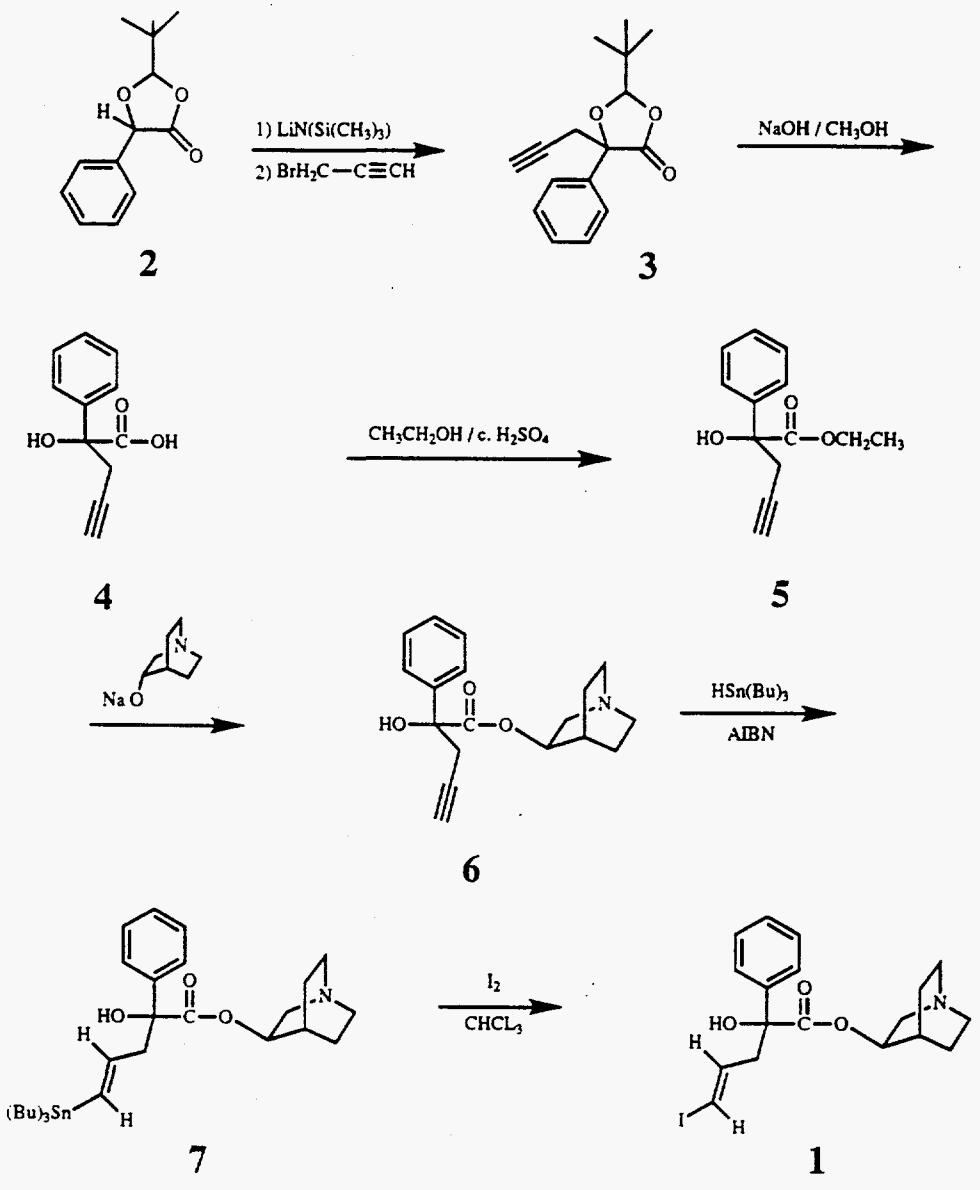


Figure 5. Stereoselective synthesis of (2S,5S)-2 and (2R,5R)-2.

E-R,S-and E-R,R-**1** allowing the determination of the enantiomeric excess of the alkylation product with propargyl bromide (**2**). **E-(R,R)-** and **E-(R,S)-1** were prepared as previously and HPLC analysis (Waters Novapak column, mobile phase:methylene chloride:ethanol:triethylamine [97:2:0.02]) of the IQNP isomers showed the alkylation did occur on the least hindered side with 94% and 98% enantiomeric excess, respectively. Purification of the E-tributyltin intermediates (**R,R-** and **R,S-7**) prior to treatment with iodine afforded **E-(R,R)-** and **E-(R,S)-1** in 95% and 99% enantiomeric excess, respectively (Figure 6). In addition, NMR analysis of **E-(R,R)-** and **E-(R,S)-1** showed a significant difference in the spectra of the region between 2.5 ppm and 2.0 ppm (Figure 7). This apparent difference in the splitting pattern for the hydrogens α to the quinuclidinyl nitrogen was also utilized to confirm the orientation of the acetate center as being R or S.

In conclusion, a facile stereoselective synthesis of α-hydroxy-α-(1-propyn-3-yl)-α-phenylacetic acetic (**4**) has been developed, allowing determination of the (R/S) conformation at this center. In addition, comparison of the specific rotation, HPLC and NMR data of **E-(R,R)-** and **E-(R,S)-1** to those prepared by the acetate moiety allows assignment of **E-(R,R)-**IQNP as the isomer demonstrating binding to the M_1 mAChR subtype and **Z-(R,R)-**IQNP as the isomer to both the M_1 and M_2 mAChR subtypes.

Table 3. Comparison of the Specific Rotation[a] Values of the E Isomers of IQNP and Intermediates.

Compound	Stereoselective Synthesis °C	Classical Resolution[b]
(R,R)-2 (S,S)-2	(-)82.4° (+)87.3°	******* *******
(R,R)-3 (S,S)-3	(+)27.2° (-)27.8°	******* *******
(R)-4 (S)-4	(-)20.6° (+)20.8°	-10.7° +12.7°
(R)-5 (S)-5	(-)24.9° (+)25.2°	-13.6° +18.4°
(R,R)-6 (S,S)-6	(-)13.4° (+)40.6°	-4.5° +41.8°
E-(R,R)-7 E-(R,S)-7	(-)17.5° (+)30.7°	-12.5° +29.0°
E-(R,R)-1 E-(R,S)-1	(-)17.4° (+)42.4°	-20.2° +39.5°

[a] Rotation measured in chloroform.
[b] Reference 28.
[c] Literature value = + 88.5°.

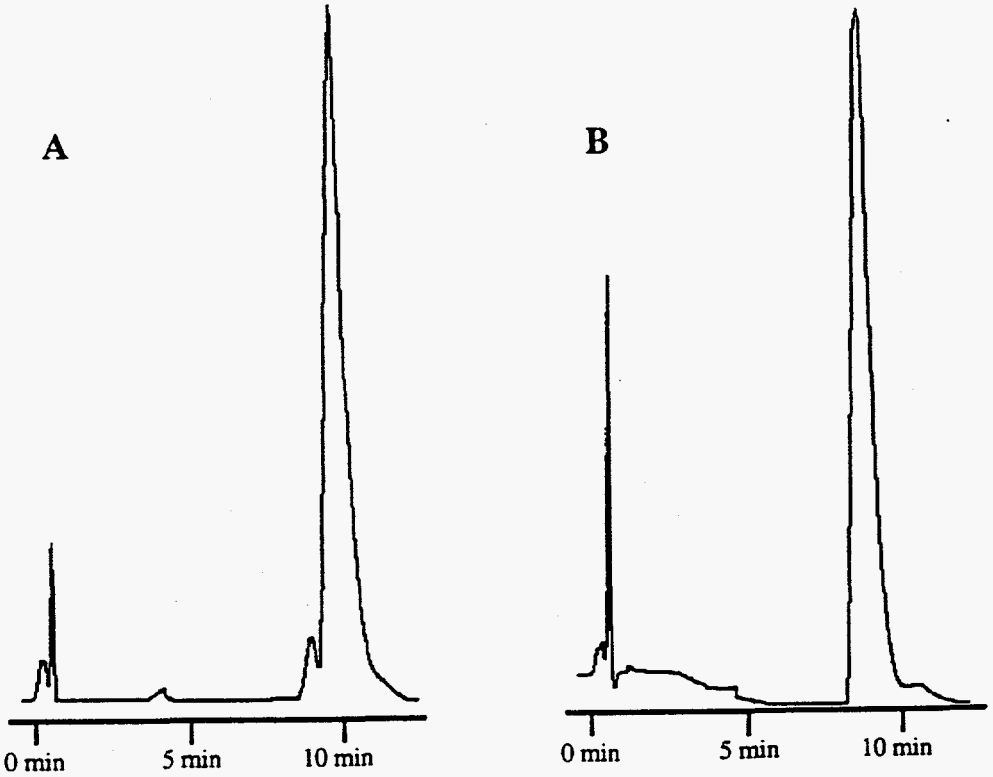


Figure 6. HPLC Analysis of **E-(R,R)**-IQNP-(A) and **E-(R,S)**-IQNP (B).

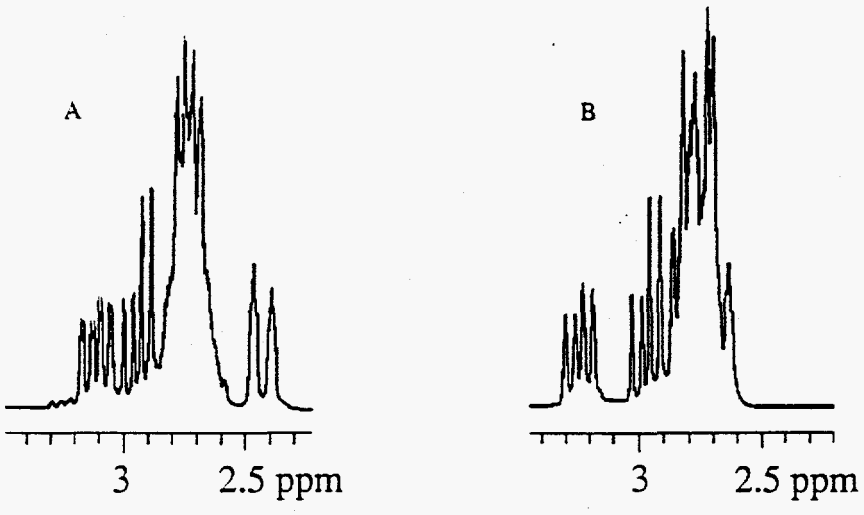


Figure 7. Selected regions of the proton NMR spectra of E-(R,R)-**1** and E-(R,S)-**1**.

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Other Nuclear Medicine Group Activities

Medical Cooperative Programs

During this period several radioisotope generators and other medical radioisotopes were provided to collaborators for joint research and included tungsten-188/rhenium-188 generators which were provided to Columbia University, New York, University of Alabama Medical School in Birmingham, Alabama, and the Beijing Normal University, in Beijing, China. In addition, tungsten-188 sodium tungstate solution was provided to the Nuclear Research Center in Shanghai, China, for fabrication of tungsten-188/rhenium-188 generators for research projects for rhenium-188-labeling of therapeutic agents.

Distribution of Radioisotopes By Cost Recovery Through the ORNL Isotopes Distribution Office (IDO)

Medical radioisotopes which were provided for full cost recovery through the ORNL Isotope Production and Distribution Program included samples of high specific activity rhenium-186 which were provided to prospective customers to assess the radiolabeling efficiency of this radioisotope produced in the ORNL HFIR. Organizations included Mallinckrodt Diagnostica, in Petten, Holland, Mallinckrodt Medical, in St. Louis, Missouri, and NeoRx, Inc., in Seattle, Washington. In addition, tungsten-188/rhenium-188 generators were sold to Austin Hospital in Melbourne, and ANSTO, in Sydney, Australia.

Recent Publications

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S.-J. Wang, W. Y. Lin, M.-N. Chen, B.-T. Hsieh, L.-H. Shen, Z.-T. Tsai, G. Ting and F. F. Knapp, Jr., "Biodistribution of Rhenium-188 Lipiodol Infused via the Hepatic Artery of Rats with Hepatic Tumors," Eur. J. Nucl. Med., 23, 13-17 (1996).

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Meetings

American Chemical Society Participation

Members of the Nuclear Medicine Group participated in the 211th Annual Meeting of the American Chemical Society held in New Orleans, Louisiana, during the March 24-29 period and co-authored an oral paper in the Medicinal Chemistry Section (Luo, et al.) And a poster presentation in the Organic Chemistry Section (Lin, et al.). The poster was also chosen for presentation as one of 50 posters in the multi-disciplinary "SciMix" session.

Luo, H., McPherson, D. W. and Knapp, Jr., F. F., "Synthesis of four stereoisomers of FQNPe: Potential Imaging Ligands for the Muscarinic-Cholinergic Receptor (mAChR) by PET."

Lin, Q., Luo, H., Mokler, F., McPherson, D. W., and Knapp, Jr., F. F., "Preparation of the 3R- and 3S-methyl Isomers of the Myocardial Imaging Agent, BMIPP."

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