



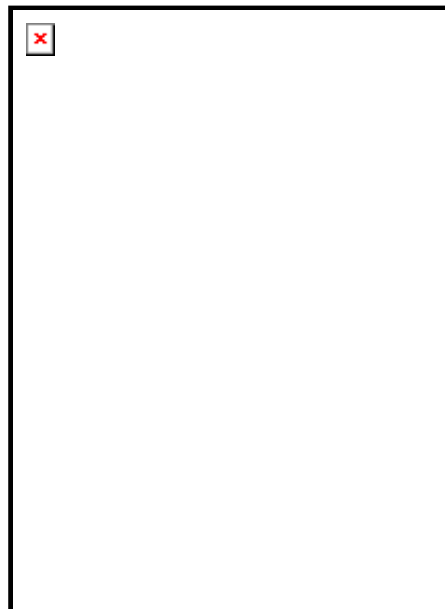
# International Isotope Society

Northeast US Chapter Meeting, October 24-24, 1996 in Mystic, CN

..ORAL PRESENTATIONS..POSTER PRESENTATIONS..

## ORAL PRESENTATIONS

- [Vicinal Polycarbonyls and Related Intermediates](#)
- [Development and Application of a Novel Method for C-14 Labeling of Cyclic Enones](#)
- [Synthesis and Applications of High Specific Activity \[<sup>35</sup>S\]-Sulfonamide Radioligands](#)
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- [Scintillation Proximity Assay, A Versatile Radioisotopic Technique](#)
- [Radiometric Flashplate Applications for High Throughput Screening](#)



## POSTER PRESENTATIONS

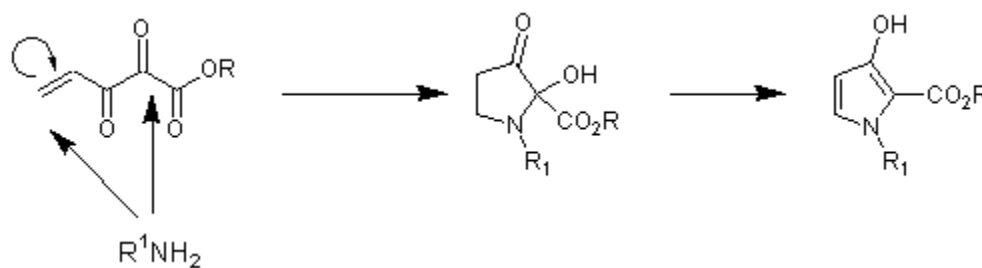
- [Preparation of \[<sup>14</sup>C\]-Labeled MLS-337](#)
- [Suzuki Cross-Coupling for the Incorporation of Labeled Methyl Groups onto Aryl Halides](#)
- [Palladium-Catalyzed Aryl Cyanations in the Radiosynthesis of \[<sup>14</sup>C\]-Labeled Pharmaceuticals](#)
- [Sensitive, Accurate Quantification of Radiolabeled Samples on TLC Plates](#)
- [Oxidation and Extraction of Organic Solvents in Tritiated Mixed Wastes: An Evaluation of Options](#)
- [Dual Selective Detection of \[<sup>13</sup>C\] and \[<sup>15</sup>N\] Stable Isotope Labeled Drug](#)
- [S.U.P.E.R. Isotopic Labeling of Natural Products](#)
- [Pollution Prevention Opportunity Assessment for Radioactive/Mixed Wastes](#)

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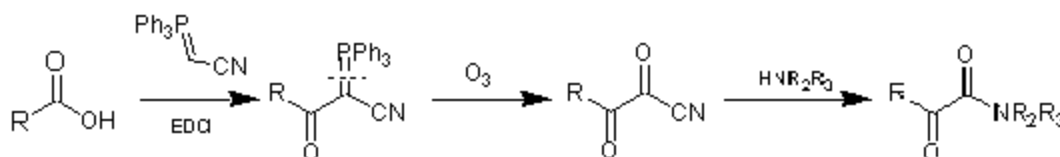
### **Vicinal Polycarbonyls and Related Intermediates. Application in the Synthesis of Bioactive Systems.**

Harry H. Wasserman  
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Useful methods for the preparation of vicinyl tricarbonyls and related cyano derivatives have been developed from readily available starting materials. When conjugated with double or triple bonds, the tricarbonyls form new functional group aggregates which may serve as di- or tri- electrophiles in the synthesis of heterocyclic systems.



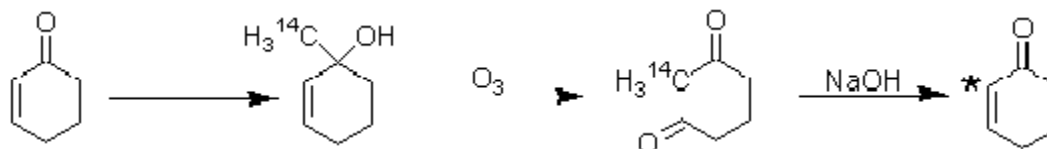
In a particularly useful procedure, carboxylic acids are converted to cyanophosphoranes which on oxidation yield diacyl nitriles. These very reactive species may be trapped with various nucleophiles such as water, alcohols or amines. The reaction with amines yields  $\mu$ -keto amides which are of timely interest as protease inhibitors.



### Development and Application of a Novel Method for the Carbon-14 Labelling of Cyclic Enones

Keith McCarthy, Kathleen Zandi and Michael DeNinno  
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A novel method for the carbon-14 labelling of cyclic enones has been developed. The key steps involve the 1,2-addition of [ $^{14}\text{C}$ ]-methyl Grignard to the enone followed by the "anomalous" ozonolysis of the resulting allylic alcohol utilizing a non-traditional basic work-up. In this two step procedure, the original enone is regenerated with a [ $^{14}\text{C}$ ] carbon atom at the alpha position. This new protocol provides modest to good yields of labelled enones and may prove to be more widely applicable than the classical Fujimoto-Belleau procedure. The details of this chemistry and its application to the synthesis of the cholesterol absorption inhibitors [ $^{14}\text{C}$ ]-CP-148,623 and [ $^{14}\text{C}$ ]-CP-242,184 will be described.

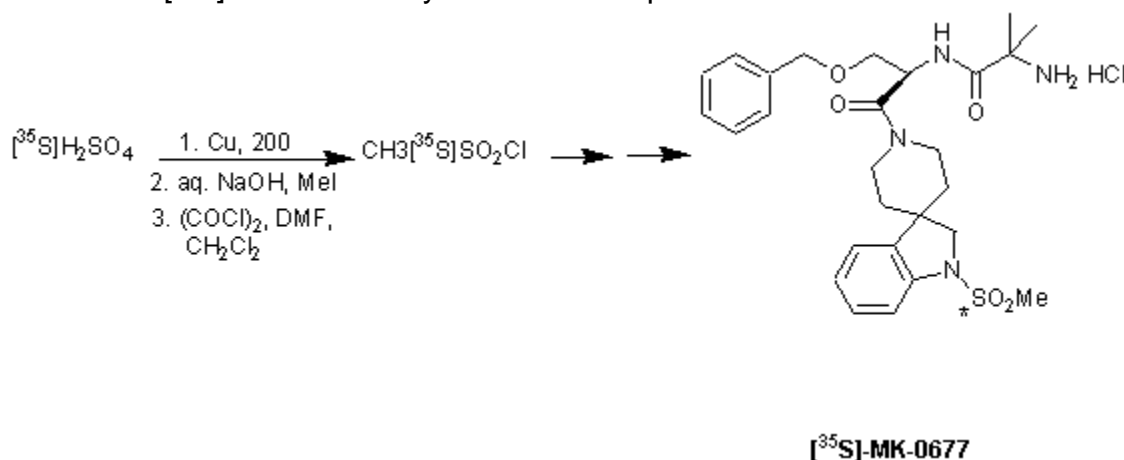


### Synthesis and Application of High Specific Activity [ $^{35}\text{S}$ ]Sulfonamide Radioligands

Dennis C. Dean  
Merck Research Laboratories

Rahway, NJ

The requirement for more sensitive high affinity probes for receptor and enzyme targets has placed new demands on radioligands. Tritium cannot offer high enough specific activity, while iodine-125 frequently adversely affects binding affinity and lipophilicity of small molecules. As an alternative labeled functionality, we have developed methodology to prepare carrier-free [<sup>35</sup>S]sulfonamide radioligands with specific activities in excess of 1000 Ci/mmol using methane [<sup>35</sup>S]sulfonyl chloride, which is readily obtained from [<sup>35</sup>S]sulfuric acid as shown below. This approach was initially used to prepare [<sup>35</sup>S]MK-0677 which was invaluable for identification and cloning of a new receptor involved in the regulation of growth hormone release. Details of the synthesis, characterization and stability of this radioligand, along with new extensions and applications of the [<sup>35</sup>S]sulfonamide synthesis will be presented.



### Accelerator MS in Bioscience Research: Attomoles and FemtoCuries

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Lawrence-Livermore National Laboratory  
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Accelerator MS (AMS) uses high energy ions, mass spectrometric separation, and nuclear counting techniques to provide identification and quantification of radioisotopes having half-lives between 10 and 10<sup>-7</sup> years to attomole sensitivity in sub-milligram-sized samples. Radiocarbon, tritium and <sup>129</sup>I provide labels to make stable and/or exact-analog chemical compounds for assays and long duration in vivo studies at levels 10<sup>-6</sup> times lower than achieved with other methods. Hyphenated AMS has been used to determine metabolites and active chemical species that bind to specific proteins or DNA at doses equivalent to a single cigarette or a single bite of cooked red meat. Many trace nutrient or toxic elements have long-lived radioisotopes that are available for tracing through AMS. With lifetimes longer than the human "three score and ten" by many orders of magnitude, these are used to trace physiological chemistry at safe chemical and radiological doses. Results from organic and elemental tracing experiments will be discussed along with a survey of the instrumental method and the prospects for wider applications using a new generation of spectrometers being developed for biochemical laboratories.

## Direct Labeling of Multifunctional Compounds by Organoiridium Catalysis using Deuterium or Tritium Gas

W. Chen, K.T. Games, S.H. Levinson, J.F. Mack, A. Mahoney, D. Saunders, S.G. Senderoff, A.Y.L. Shu, A.J. Villani and J.R. Heys\*  
Radiochemistry, SmithKline Beecham Pharmaceuticals  
P.O. Box 1539, King of Prussia, PA 19406

Recent communications from these laboratories (1) and others (2) have described the exchange labeling of a variety of compounds using deuterium or tritium gas, catalyzed by several organoiridium complexes. Our initial work was inspired by observations of the reactivity of  $[\text{IrH}_2(\text{acetone})_2(\text{PPh}_3)_2]\text{BF}_4$  (1) by Crabtree (3). The exchange we observe is often rapid, efficient and highly regioselective, and proceeds under very mild conditions (room temperature, less than one atmosphere of deuterium or tritium gas). Regioselectivity of exchange is associated with several functional groups, and the proposed mechanism of exchange, involving initial coordination of the metal center to the functional heteroatom followed by oxidative addition to the activated C-H bond, is supported by spectroscopic and structural studies of reactions and isolated intermediates. The method is usually selective for aryl C-H bonds, but certain structural features promote labeling of specific aryl sites. Modifications of the phosphine ligands on iridium influence the rate and selectivity of exchange, and some of our results indicate that regioselectivity in labeling can be controlled by choice of organoiridium complex and reaction conditions. The tritium exchange labeling of a variety of complex compounds is achieved in the presence of complex 1 or catalyst precursors  $[(\text{cod})\text{IrL}_2]\text{X}$  (L = various mono- and bidentate phosphines, X =  $\text{BF}_4$  or  $\text{PF}_6$ ) and tritium gas. High specific activity levels are often achieved; however, larger amounts of complex are usually required for successful labeling of multifunctional compounds than for simple model compounds. Data on reaction order suggest that quite small amounts of labeling gas can be used to achieve significant amounts of label incorporation into substrate. The body of results obtained to date 1) allow prediction of the feasibility and regioselectivity of labeling of compounds of interest, based on their chemical structures; 2) provide emerging capability to control labeling, reoselectivity; and 3) show functional group tolerance largely complementary to that of traditional heterogeneous catalysts. Together, these developments provide a powerful method for the rapid provision of high quality labeled compounds for a wide range of uses.

(1).Heys, J.R. - *J. Chem. Soc. Chem. Commun.* 680 (1992); Heys, J.R., in Synthesis and Applications of Isotopically Labelled Compounds 1991, E. Buncl and G.W. Kabalka, Eds., Elsevier, Amsterdam, 1992, pp. 52-7; Heys, J.R., Shu, A.Y.L., Senderoff, S.G. and Phillips, N.M. - *J. Lab. Comp. Radiopharm.* 33: 431 (1993); Shu, A.Y.L. and Heys, J.R. - *ibid.* 34: 587 (1994); J.R. Heys, A.Y.L. Shu and L.E. Nice, in Synthesis and Applications of Isotopically Labelled Compounds 1994. J. Allen and R. Voces, Eds., Wiley, West Sussex, 1995, pp. 175-180; A.Y.L. Shu, W. Chen and J.R. Heys - *J. Organometal. Chem.*, in press; W.Chen, et al. - *J. Lab. Comp. Radiopharm.*, submitted.

(2).D. Hesk, P.R. Das and B. Evans, *J. Lab. Comp. Radiopharm.*, 36 (1995) 497.

(3).R.H. Crabtree, et al. - *Inorg. Chem.* 1985, 24, 1986.

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### Seven Years Exploration of New Tritium Labelling Methods

Hendrik Andres, Nicholas DeMello, David R. Goodlett, Devendra K. Jaiswal, Hiromi Morimoto, Henry Rapoport, Manouchehr Saljoughian, Chit Than, Richard B. van Breemen, Philip G. Williams and Elizabeth M. Zippi

National Tritium Labelling Facility and Structural Biology Division, Lawrence Berkeley National Laboratory, Mailstop 75-123, One Cyclotron Road, Berkeley, CA 94720, U.S.A.

A great deal of elegant chemistry is available for hydride transfer reactions, and could be adapted for tritium labelling. Nevertheless, most high level tritiation reactions still involve either hydrogenation (alkene or alkyne precursor) or catalytic dehalogenation. In the last seven years we have endeavoured to propose and popularize alternative labelling techniques and reagents, including i). the synthesis of new precursors for the production of methyl iodide<sup>1</sup>; ii). the synthesis of methylene diiodide<sup>2</sup>; iii). the production and use of T<sub>2</sub>O, and solvents made from it e.g. CH<sub>3</sub>COOT, CF<sub>3</sub>COOT; iv). high specific activity hydride reagents e.g. LiAlT<sub>4</sub>, <sup>3a</sup> Li(OCH<sub>3</sub>)BT,<sup>3a</sup> (n-Bu)<sub>3</sub>SnT, ZrCp<sub>2</sub>CIT,<sup>3c</sup> LiT,<sup>3d</sup> Li(OCH<sub>3</sub>)<sub>3</sub>BT,<sup>3d</sup> Ph<sub>2</sub>SiT<sub>2</sub>,<sup>3e</sup> BT<sub>3</sub>-THF,<sup>3f</sup> Li/Na/KBT<sub>4</sub> v) reduction with dimide;<sup>4</sup> vi). use of T<sub>2</sub>O in special reactions such as the Shapiro reaction<sup>5</sup> and Brook rearrangement;<sup>6</sup> and vii). development of a new acetylation reagent.<sup>6</sup> We have also initiated and continued a number of innovative applications of tritium NMR spectroscopy.

Many of these projects have grown out of User or Collaborator requirements at the NTLF. We regard this stimulus to develop and refine both tritiation and NMR techniques as healthy and challenging.

#### References

- 1.M. Saljoughian et al, *J. Chem. Soc., Perkin Trans. I.*, 1990, 1803-1808.
- 2.M. Saljoughian et al, *J. Chem. Soc., Chem. Commun.*, 1990, 1652-1653.
- 3.(a) H. Andres et al., *J. Chem. Soc., Chem. Commun.*, 1990, 627; (b) D.K. Jaiswal et al, *J. Chem. Soc., Chem. Commun.* 199'D, 907; (c) E.M. Zippi et al, *Synth. Commun.*, 1994, 24, 1037-1044; (d) E.M. Zippi et al., *Synth Commun.*, 1995, 25, 2685-2691; (e) E.M. Zippi et al., manuscript in preparation; (f) C. Than *et al.*, *J. Org. Chem.*, 1995, 60, 7503-7507, C. Than et al., *J. Labelled Radiopharm. Compd.*, 1996, 38, 693-711.
- 4.M. Saljoughian *et al.* *J. Chem. Soc. Chem. Commun.*, 1993, 414.
- 5.M. Saljoughian *et al.* *Tetrahedron Lett.*, 1996, 37 (17), 2923-2926.
- 6.M. Saljoughian *et al.* manuscripts in preparation.

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### Scintillation Proximity Assay, A Versatile Radioisotopic Technique for High Throughput Drug Screening

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Research and Development  
Amersham International plc,  
Cardiff, Wales, United Kingdom

Scintillation Proximity Assay (SPA) is a radioisotopic assay technology that has been shown to be widely applicable in radioimmunoassay (RIA), receptor binding assays and enzyme assays. The SPA principle relies on the observation that in aqueous solution, weak β-emitters, such as <sup>3</sup>H, need to be close to scintillant molecules to produce light, otherwise the energy is lost to the solvent. By coupling specific molecules to the scintillant containing SPA beads, a range of homogeneous drug screening assays can be constructed which require no separation step, as

only radioligand in close proximity to the bead generates a light signal. Examples of the use of this enabling technology in developing drug screening assays will be presented.

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## Radiometric FlashPlate<sup>®</sup> Applications for High Throughput Screening

Simon C. Ng, Beverly A. Brown, Deb Curran, Sharon Tompkins, Georgette Henrich, Sally Casto, and Harry Hamey  
NEN<sup>™</sup> Life Sciences Inc.  
549 Albany Street, Boston, MA 02118

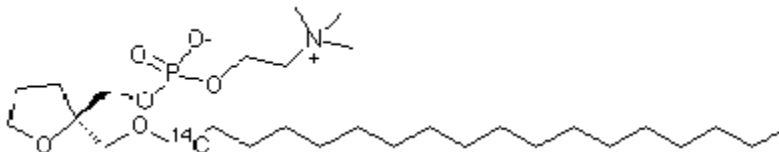
FlashPlate<sup>®</sup>, a 96 well microplate precoated with a thin layer of plastic scintillant, can be useful in detecting  $\beta$  emitting isotopes such as <sup>3</sup>H, <sup>33</sup>P, <sup>14</sup>C and <sup>125</sup>I. This type of assay format eliminates the addition of liquid scintillant and it is easily adaptable to automation for greater high throughput screening capability. The working mechanism in this type of platform is based on an immobilized molecule on the surface of the well capturing a radiolabeled ligand in solution which results in detection of the bound radioactivity. In general, uncaptured radiolabeled ligand will not be detected due to its distance away from the scintillant. Therefore, separation steps may not be necessary with most isotopes. A variety of radiometric assays such as enzymatic assays, live cell assays and radioimmunoassays (RIAs) can be simplified by this platform. Enzymatic assays for measuring activity of helicase, reverse transcriptase, protein kinases and chloramphenicol transferase (CAT) are feasible on FlashPlate<sup>®</sup>. Several established cell lines have been shown to grow and attach to FlashPlate<sup>®</sup>, which allows for rapid detection of radiolabeled ligand in a live cell based environment. Several RIAs have been optimized on FlashPlate<sup>®</sup> and the assays have comparable performance to assays done by standard methods. Therefore, FlashPlate<sup>®</sup> is an extremely versatile platform well suited for a broad range of high throughput screening applications.

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### Preparation of [<sup>14</sup>C]-Labeled MLS-337

Grazyna Ciszewska and Ustun B. Sunay  
Radiosynthesis Group, Chemical Research and Development  
Sandoz Research Institute, East Hanover, NJ 07936

MLS-337, a new Multiple Sclerosis candidate, labeled with [<sup>14</sup>C] was required for pharmacokinetic ADME studies.



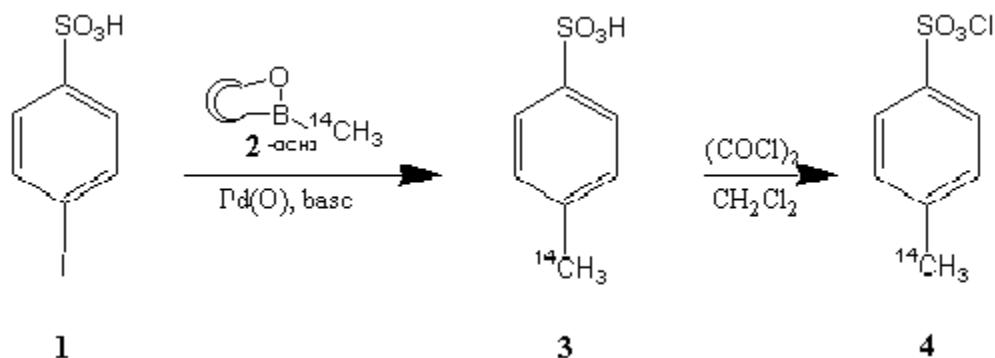
The title compound was constructed in a convergent manner, utilizing 1-[<sup>14</sup>C]octadecylbromide and (r)-tetrahydro-2-[(phenylmethoxy)methyl]-2-furanmethanol. The alkyl bromide was obtained in the following manner: treatment of 1-bromoheptadecane with K<sup>14</sup>CN gave labeled alkyl nitrile, which was hydrolyzed to the acid by the action of acetic acid/ sulfuric acid/ water. The carboxyl function was next converted in two steps to the required [<sup>14</sup>C]bromo intermediate.

The benzyl-protected labeled ether was synthesized by coupling of the protected chiral tetrahydrofuran dimethanol with alkylating agent. Deprotection was straightforward and drug substance was obtained in a three-step, one pot operation.

### Suzuki Cross-Coupling for the Incorporation of Labeled Methyl Groups onto Aryl Halides A Novel Synthesis of [4-Methyl- $^{14}\text{C}$ ]Tosyl Chloride

Matt Brown, Dennis Dean and Dave Melillo  
Department of Drug Metabolism  
Merck & Co  
Rahway, NJ 07065

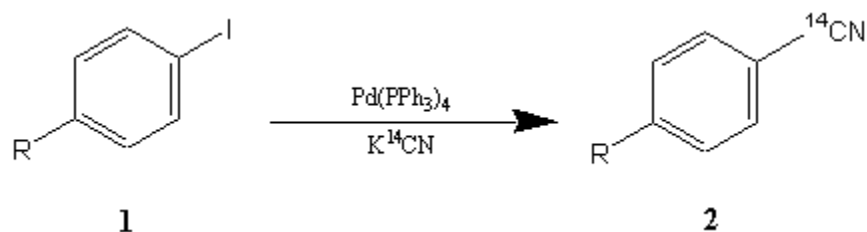
A novel synthesis of [4-methyl- $^{14}\text{C}$ ]tosyl chloride **4** has been developed which utilizes a Suzuki cross coupling between aryl halide **1** and labeled methylborane **2** as the key step. This process avoids the poor regioselectivity typically attendant with aromatic sulfonation. The generality of this process as a method for the incorporation of labeled methyl groups will be considered as will the effects of various reaction parameters.



### Palladium-Catalyzed Aryl Cyanations in the Radiosynthesis of [ $^{14}\text{C}$ ]-Labeled Pharmaceuticals

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Ciba Pharmaceuticals Division  
Summit, NJ 07901

The introduction of [ $^{14}\text{C}$ ]-labeled cyano substituents onto aromatic rings is a valuable tool in the synthesis of labeled drug candidates used in metabolism and pharmacokinetic studies. We have found that the palladium-catalyzed reaction of aryl iodides **1** with [ $^{14}\text{C}$ ]-labeled cyanide offers an efficient and versatile method for the preparation of [ $^{14}\text{C}$ ]-labeled benzonitriles **2**. The cyano group in **2** is readily converted to other functional groups such as aldehydes, acids and amidines. This cyanation method allows direct incorporation of labeled potassium cyanide in the presence of other functionalities (R = chloride, silyl ethers, alkoxides, amides) providing distinct advantages over other methods such as the Rosenmund cyanation reaction. The benzonitrile products were used in the radiosynthesis of [ $^{14}\text{C}$ ]-labeled pharmaceuticals including a new  $\text{LTB}_4$  antagonist and a novel anti malarial drug. These applications of the method, and related developmental work will be described.



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### Sensitive, Accurate Quantification of Radiolabeled Samples on TLC Plates with Electronic Autoradiography

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Packard Instrument Company  
Meriden, CT

The purpose of this study was to validate the use of direct beta detection with the InstantImager Electronic Autoradiography System for the detection and quantitation of radiolabeled metabolic products separated by thin layer chromatography. The intent was to qualify the InstantImager to replace the traditional method of scraping samples from a plate into vials for counting by liquid scintillation counting. The performance is defined in terms of sensitivity and accuracy.

Samples were quantified using several different acquisition times on the InstantImager to determine thresholds of detection with respect to count time. The identical samples were quantified by traditional liquid scintillation counting methods to determine the accuracy and counting efficiency. The results indicate that the detection threshold of the InstantImager for [<sup>14</sup>C] is less than 1.0 dpm/mm(2) in 30 minutes and as low as 0.2 dpm/mm(2) in 16 hours. The R2 values for the linear regression of the CPM results of the InstantImager with data from traditional liquid scintillation counting were 0.99.

Based on these results, the InstantImager performs with superior sensitivity and accuracy for the quantification of radiolabeled material separated by thin layer chromatography. Ease of use and data handling in the form of image files makes this instrumentation particularly useful for the quantitation of radiolabeled samples separated by thin layer chromatography. Applications for quantification of soil metabolites and radiochemical synthesis monitoring are described to illustrate practical use of the InstantImager.

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### Oxidation and Extraction of Organic Solvents in Tritiated Mixed Wastes: An Evaluation of Options

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Li-Yang Chang, EH&S Div.  
Lawrence Berkeley National Laboratory  
University of California  
Berkeley, CA 94720

LBNL is conducting a treatability study on tritiated mixed waste samples. This treatability study is designed to evaluate the effectiveness and efficiency of treating mixed waste with thermal

treatment technologies, in order to generate non-hazardous low-level radioactive waste by-products.

**Catalytic Chemical Oxidation Process.** The NTLF at LBNL has constructed a CCO system for the treatment of tritiated mixed waste. Several tests have been conducted with surrogate liquid waste streams. Samples were pumped through a preheater (at 300-350 C), an oxidation chamber (at 400-550 C) with oxygen inflow at 4 l/min, and a catalytic reactor filled with platinum coated alumina pellets (at 500 C). The liquid flow rates were controlled in the range of 1.5 to 2 mL/min. Water and other reaction products were effectively collected using a series of condensers and a dry-ice cold trap.

Surrogate hazardous waste streams consisting of (1) water solutions containing 70% methanol, and (2) water solutions containing 90% acetonitrile have been processed through the system. During sample (1) treatment, a maximum of 8 ppm CO was detected in the exhaust gasses, while no CO was observed during sample (2) oxidation. The treatment products were also analyzed with a GC/MS system. For sample (1), only trace amounts of benzaldehyde and less than 5 ppm of acetaldehyde were detected. For sample (2), neither acetonitrile nor any oxidation products were detected in the ppm range.

The other technologies which will be evaluated are the Molten Salt Oxidation (MSO), and Supercritical Water Oxidation (SCWO) processes. The extraction of organic solvents from tritiated water or silica gel with supercritical CO<sub>2</sub> (SCCO<sub>2</sub>) will also be evaluated.

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### **Dual Selective Detection of [<sup>13</sup>C] and [<sup>15</sup>N] Stable Isotope Labeled Drug in Whole Urine and Serum Using Continuous Flow-Isotope Ratio Mass Spectrometry for Mass-Balance Studies**

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Boston University School of Medicine and  
Veterans Affairs Medical Center, Boston and  
MassTrace, Woburn MA

**BACKGROUND.** We are developing stable isotope methods for performing mass balance studies traditionally done with radioactive tracers.

**METHODS.** Three subjects received 650 mg equivalents of [<sup>15</sup>N <sup>13</sup>C] acetaminophen p.o. and 24 hour urines were collected for 72 hours. Serial serum samples (0-24 hrs) were obtained from one subject. Stable isotope labeled drug was measured in urine and serum by the dual selective detection of [<sup>15</sup>N] label in N<sub>2</sub> gas and subsequent [<sup>13</sup>C] label in CO<sub>2</sub> gas from dry, on line Dumas combustion of single whole matrix samples.

**RESULTS.** Coefficients of determination [R<sup>2</sup>] values of 0.99+56 to 1.0000 were obtained for the standard curves. Urine recovery (72 hrs) were 1) 97.4 (<sup>13</sup>C<sub>2</sub>), 90.3 (<sup>15</sup>N); 2) 78.9 (<sup>13</sup>C<sub>2</sub>), 77.0 (<sup>15</sup>N); 3) 95.4 (<sup>13</sup>C<sub>2</sub>), 90.6 (<sup>15</sup>N). The serum pharmacokinetic values determined (total label, drug and metabolites) from subject one were: Vd (L/KG) 0.406 (<sup>13</sup>C<sub>2</sub>); 0.383 (<sup>15</sup>N); CL (L/KG/HR) 0.072 (<sup>13</sup>C<sub>2</sub>); 0.087 (<sup>15</sup>N); T<sub>1/2</sub> (HRS) 3.9 (<sup>13</sup>C<sub>2</sub>); 3.1 (<sup>15</sup>N).

We present evidence that 1) stable isotope (<sup>13</sup>C or <sup>15</sup>N)/CF-IRMS methods possess sufficient sensitivity, precision, and accuracy for performance of mass balance studies; 2) Such studies can be successfully carried out in man.

## S.U.P.E.R. Isotopic Labeling of Natural Products

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Department of Chemistry  
University of Rhode Island

Exchange reactions between isotopic hydrogen donors and organic substrates remains an important goal in biosynthetic and organic synthetic chemistry. In particular, deuterium ( $^2\text{H}$ ) and tritium ( $^3\text{H}$ ) labeling of simple to complex carbohydrates, and carbohydrate moieties of glycoproteins and glycolipids, continues to engender major effects in bioorganic chemistry. Recent efforts have resulted in the further development and extension of a facile labeling technique, which affords stereospecific  $^1\text{H}\rightarrow^2\text{H}$  (or  $^1\text{H}\rightarrow^3\text{H}$ ) isotopic exchange, under very mild conditions, which is facilitated by ultrasonic irradiation (Stereospecific Ultrasonically Promoted Exchange Reaction, or "S.U.P.E.R."). Ultrasonic irradiation promotes stereospecific exchange, without the attendant degradation or racemization of thermally labile natural products as observed by others when conducted at higher temperatures and long incubation periods. By choosing a small number of simple to complex compounds, a combinatorial approach has been used to evaluate the reaction, the potential applications, possible general synthetic utility, and functional group limitations. This technique has been successfully extended to include such biomolecular classes as anti-malarial agents, anti-tumor agents, anti-bacterial agents, and cardiac glycosides. Further research is underway to extend this technique for complex structural determination and MRI imaging.

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## Pollution Prevention Opportunity Assessment for Radioactive/Mixed Wastes Generated by Biomedical Research.

Li-Yang Chang, EH&S Div.  
H. Morimoto and PG Williams, National Tritium Labeling Facility  
Lawrence Berkeley National Laboratory  
University of California  
Berkeley, CA 94720

"Can low-level radioactive/mixed wastes be managed, treated or reduced out of existence?" Today, in the United States, the radioactive or mixed wastes generated by biomedical R&D community is faced with limited or no disposal options. This is why we conducted the radioactive waste pollution prevention opportunity assessment for the life science and structural biology researcher in the Berkeley Laboratory.

Methodology of the Assessment. The approaches included 1) identification of the LL radioactive and mixed wastes generation processes through generator interview, 2) constructing the process flow diagram for each waste stream, 3) characterizing those identified waste streams, and 4) identifying potential waste stream disposal, treatment, and reduction opportunities and regulatory constraints.

Description of Various Waste Processes. The numerous experiments or processes that generate LL radioactive and mixed wastes includes (A) DNA and RNA Labeling, Hybridization, and Sequencing, (B) Protein, Cell, or Blood Sequencing or Culturing, and (C) Biomedical Chemical Synthesis, and Medicine Labeling. Within these three categories, they have the following processes: (1) DNA and RNA labeling and sequencing using  $^{32}\text{P}$  or  $^{35}\text{S}$ ; (2) Southern and Northern Blot hybridizations using  $^{32}\text{P}$  or  $^{35}\text{S}$ ; (3) DNA extraction and precipitation; (4) CsCl gradient fractionation of DNA; (5) DNA repair studies using  $^3\text{H}$ ,  $^{14}\text{C}$ , or  $^{32}\text{P}$  labeled DNA; (6) protein sequencing of red blood cells using  $^{32}\text{P}$ ; (7) culturing tissue cells using tritium to study

cell transformation; (8) cholesterol studies with  $^{14}\text{C}$  and triglycerides study with tritium; (9) blood plasma labeling with  $^{14}\text{C}$  and/or tritium; (10) protein labeling with  $^{125}\text{I}$ ; (11) radiolabeling pharmaceuticals and ligands with  $^{18}\text{F}$ ,  $^{125}\text{I}$ ,  $^{123}\text{I}$ - and tritium; and (12) PET and SPECT tomographic study with animals using  $^{18}\text{F}$  or  $^{123}\text{I}$ .

**Current Radioactive/Mixed Waste Reduction Options and Constraints.** The following options were identified. [1] Changing from a nitrocellulose filter to a nylon membrane. eliminating the use of formamide; [2] Radioactive wastes containing  $^{32}\text{P}$  are amenable to declassification through natural decay; [3] Liquid scintillation cocktails and buffer solution containing tritium or  $^{14}\text{C}$  as the only radioactive component might be treated with the chemical catalytic oxidation, steam reforming, or supercritical water oxidation process; [4] Changing methanol to ethanol or substituting the radiolabeling technique with the newly developed YOYO or TOTO imaging process; [5] Tissue culture with tritium can be replaced by the Immunological assays; [6] Eliminating the use of tritium in DNA synthesis experiments by conducting experiments with non-radioactive Luciferase assay; [7] Substituting  $^{32}\text{P}$  or  $^{35}\text{S}$  with  $^{33}\text{P}$  as the labeling reagent. In this assessment, we also identified several regulatory constraints, such as, "Waste Solvents Codes", "Treatability Study Notification", "Delisting Petition", "Treatment Variance", etc. No single generator has attempted to negotiate these legal and permitting problems.

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