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Radiochemical studies of the leaching of primary scintillator molecules from within sol–gel glasses

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Tritium labelled 2,5-diphenyloxazole ([^{3}H]-PPO, **1**) and 4-hydroxymethyl-2,5-diphenyloxazole ([^{3}H]-4-HOCH$_2$-PPO, **2**) have been prepared using a one-step metal catalysed isotope exchange procedure. Compound **1** was then encapsulated into a sol–gel glass *via* the polymerisation of tetraethyl orthosilicate (TEOS). Compound **2** was first reacted with 3-isocyanatopropyltriethoxysilane (3-ICPS) to form a functionalised silicon alkoxide precursor which has a urethane linkage ([^{3}H]-urethane **4**), and subsequently copolymerised with TEOS to form covalently bonded sol–gel glasses. The performance of the two glasses was differentiated on the basis of radioactivity leaching tests. In the case of the covalently bound version virtually no leaching occurred, thereby making it an attractive candidate for further applications.

Introduction

Whilst liquid scintillation counting has become a superb technique for measuring the radioactivity of weak β^- emitters such as ^{3}H and ^{14}C, the large volumes of radioactive waste produced constitute an ever increasing problem which we have attempted to address by preparing suitably doped sol–gel glasses. In the first case,[1] the widely used primary scintillator 2,5-diphenyloxazole was physically entrapped within a sol–gel matrix formed *via* the polymerisation of tetraethyl orthosilicate (TEOS). In the second case,[2] 4-hydroxymethyl-2,5-diphenyloxazole was first reacted with 3-isocyanatopropyltriethoxysilane (3-ICPS) to form a functionalised silicon alkoxide precursor which has a urethane linkage, and subsequently copolymerised with TEOS to form a sol–gel glass in which the primary solute is covalently bound. Both kinds of sol–gel glasses were able to measure the weak β^- radiation emitted by tritium. Nevertheless there was a big difference—leaching of primary scintillator was quite marked in the case of the physically entrapped form whereas in the covalently bound form hardly any leaching took place.

In previous studies, including ours, the question of leaching was addressed by observing changes in the ultraviolet (UV) spectra of solutions of leachant from the sol–gel glass in the presence of various solvents.[1–6] Other methods such as X-ray photoelectron spectroscopy (XPS),[1,2] fluorescence absorption,[7,8] ^{14}C radiolabelled bioassays[9] and ^{1}H NMR spectroscopy[10] have also found application in this area. All of these methods have disadvantages in terms of sensitivity, ease of use, sample throughput, long term stability, *etc.* In addition the preparation of ^{14}C-labelled compounds tends to involve multi-step procedures and is both expensive and time consuming.

In this paper we describe the development of an attractive alternative—the use of tritium labelled PPO and a PPO derivative as tracers—to monitor leaching from sol–gel glasses. This approach, which is capable of general application, clearly differentiates the primary scintillator physically entrapped in the sol–gel glass from the covalently bonded version. This radiochemical method takes advantage of two procedures/techniques—one-step metal catalysed hydrogen isotope exchange reactions[11] that can lead to regiospecific labelling, and ^{3}H NMR spectroscopy[12]—which have greatly increased the attractions of tritium as a tracer.

Experimental

Reagents and solvents, such as, 2,5-diphenyloxazole (Acros, scintillation grade), RhCl$_3$ (Aldrich, 99%), dimethylformamide (Aldrich, 99%), tritiated water (HTO, 5 Ci cm^{-3}), dichloromethane (DCM, BDH, 99%), silica gel 60 (Fluka), ethyl acetate (BDH, 99%), petroleum ether bp 40–60 °C (FSA, Fisons specified lab. Reagent), 3-isocyanatopropyltriethoxysilane (Avocado, 95%), triethylamine (Aldrich, 99%), TEOS (Aldrich, 98%), glacial acetic acid (Fisons, Anal.), absolute alcohol 100 (Hayman Ltd., 99.86%), toluene (Fisons, low in sulfur, Anal.), were used as received. THF was distilled over sodium before use. 4-Hydroxymethyl-2,5-diphenyloxazole was synthesised using the procedure described previously.[2]

^{1}H and ^{13}C NMR data were obtained on a Bruker AC300 spectrometer at 300 and 75 MHz respectively. The ^{3}H NMR (^{1}H decoupled) spectra were obtained on a Bruker AC300 spectrometer at 320 MHz. IR spectra were recorded on a Perkin Elmer System 2000 FTIR Spectrometer. Liquid scintillation counting was performed on a Packard Tri-Carb 1500 liquid scintillation analyser.

2-([2,6-^{3}H$_2$]Phenyl)-5-phenyloxazole ([^{3}H]-PPO) 1 and 2-([2,6-^{3}H$_2$]phenyl)-4-hydroxymethyl-5-phenyloxazole ([^{3}H]-4-HOCH$_2$-PPO) 2

Compounds **1** and **2** were synthesised using a one-step RhCl$_3$ catalysed tritiation procedure developed by Lockley *et al.*[11] (Scheme 1). Typically, a mixture of PPO (196 mg, 0.89 mmol), RhCl$_3$ (30 mg), HTO (10 µl) and DMF (3 ml) was frozen in liquid nitrogen, evacuated and frame sealed in a Pyrex glass tube. The tube was then heated in an oil bath at 110 °C for 48 hours. The tube was frozen in liquid nitrogen again before the seal was broken. The contents were transferred to a separation funnel containing water (10 cm^3) and dichloromethane (35 cm^3). The DCM layer was washed with water (2 × 10 cm^3) and dried over anhydrous Na$_2$SO$_4$. Removal of solvent afforded a yellow solid. Compound **1** was obtained as colourless crystals after purification using column chromatography (silica with a mixture of 1 : 2 ethyl acetate–petroleum ether bp 40–60 °C as solvent) in 83% yield. Compound **2** was prepared in a similar way in 57% yield. ^{1}H and ^{13}C NMR data of **1** and **2**, recorded in CDCl$_3$, together with the IR spectra, were identical to those obtained from the non-labelled versions

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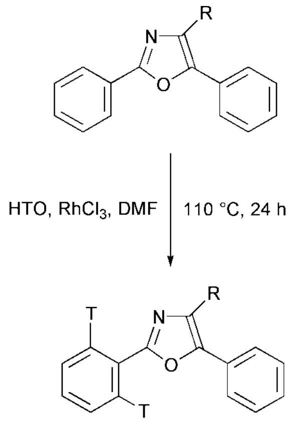


1, R = H
2, R = CH$_2$OH

Scheme 1 Rhodium trichloride catalysed homogeneous tritiation procedure.

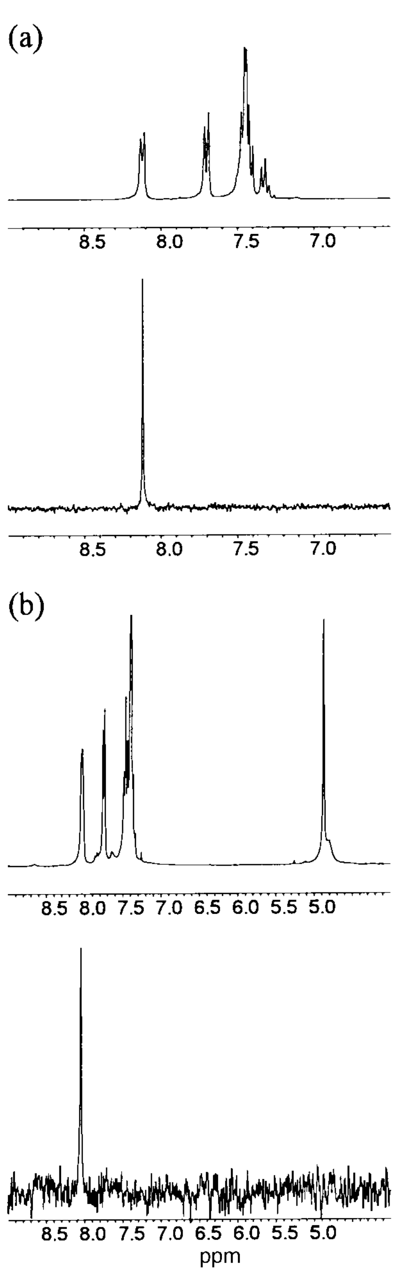


Fig. 1 ^{1}H (top) and ^{3}H (bottom) NMR spectra for **1** (a) and **2** (b).

of these compounds. The ^{3}H NMR (^{1}H decoupled) spectra were obtained in CDCl$_3$ and are shown in Fig. 1. The specific radioactivity of **1** was 574 KBq mg^{-1} and for **2**, 158 KBq mg^{-1}.

[^{3}H]-Urethane 4

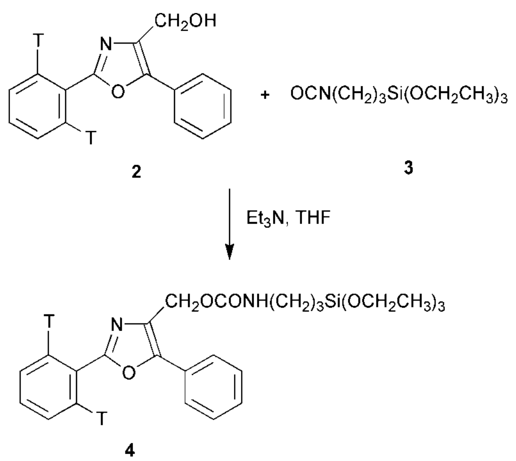
A mixture of **2** (94 mg, 0.37 mmol), 3-isocyanatopropyltriethoxysilane (0.2 g, 0.81 mmol) and triethylamine (0.06 cm^3) in THF (5 cm^3) was refluxed under nitrogen (Scheme 2). The progress of the reaction was closely monitored by following the disappearance of the peak at 2273 cm^{-1} (-N=C=O) in the infrared spectrum, and the formation of the peak at 1723 cm^{-1} (urethane). At the end of the reaction, removal of THF afforded a pale yellow solid. After purification using column chromatography (silica gel, 1 : 1 mixture of ethyl acetate and petroleum ether bp 40–60 °C as solvent) a near white waxy solid (0.14 g, 76%) was obtained. Mp 53–58 °C; δ_H (300 MHz, CDCl$_3$) 8.11 (m, 2H), 7.75 (m, 2H), 7.47 (m, 6H), 5.28 (s, 2H), 3.82 (q, 6H), 3.22 (m, 2H), 1.60 (m, 2H), 1.23 (t, 9H), 0.63 (m, 2H); δ_C (75 MHz, CDCl$_3$) 160.2, 158.1, 148.8, 132.1, 130.5, 129.0, 128.9, 128.7, 127.7, 127.1, 126.4, 126.2, 50.4, 50.2, 43.5, 23.3, 18.2, 7.6; ν_{max}(KBr)/cm^{-1} 1723 (s, -OCONH-). The specific radioactivity of **4** was 36 KBq mg^{-1}.

Sol–gel glasses doped with [^{3}H]-PPO

A stock mixture of TEOS (3.05 cm^3, 13.7 mmol), water (0.49 cm^3, 27.2 mmol), ethanol (2.41 cm^3, 41.1 mmol), acetic acid (0.06 cm^3) and [^{3}H]-PPO, **1**, (11.7 mg) was prepared. The solution was divided into 4 × 1.5 cm^3 portions, and each stored in a glass vial (10 cm^3). These vials were sealed with a screw cap then kept at room temperature to gel (1 week) and age (1 week) under ambient conditions. The gels were then allowed to dry slowly, by replacing the cap with perforated aluminium foil, at room temperature for one week, followed by drying at 70 °C overnight. The sol–gel glasses were obtained as clear, colourless monoliths.

Sol–gel glasses incorporating covalently-bonded [^{3}H]-PPO

A mixture of TEOS (1.58 cm^3, 7.0 mmol), water (0.25 cm^3, 13.9 mmol), ethanol (1.21 cm^3, 20.6 mmol), acetic acid (0.03 cm^3) and [^{3}H]-urethane, **4**, (20.9 mg) was prepared as a clear, colourless solution. The solution was divided into 2 × 1.5 cm^3 portions, and each stored in a glass vial (10 cm^3). The gelling, ageing and drying processes were similar to those used for the preparation of [^{3}H]-PPO doped sol–gel. The final sol–gel glasses were obtained as clear, colourless monoliths.



Scheme 2 Synthesis of **4**.

Leaching test

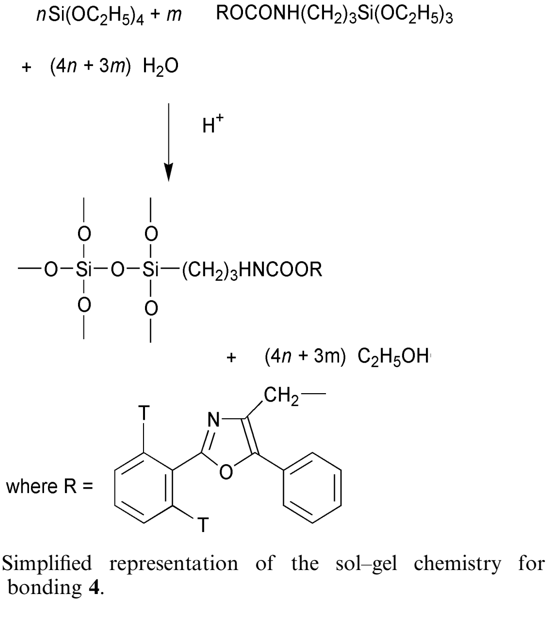
To a glass vial (10 cm^3) was added the doped sol–gel glass (60 mg), which was coarsely ground, and toluene (3.0 cm^3). The mixture was gently agitated at room temperature for at least 5 min before allowing the sol–gel glass to settle to the bottom of the vial, at which stage 10 µl of the liquid was removed and transferred to a glass vial containing liquid scintillator (Ecoscint A, 10 cm^3). This procedure was repeated at regular intervals. The vials were then counted for their radioactivity (disintegrations per minute, DPM).

Results and discussion

Comparison of the ^{1}H NMR spectrum of **1** with the ^{3}H(^{1}H decoupled) NMR spectrum (Fig. 1a) shows that the tritium has been incorporated with a 100% regiospecificity using $RhCl_3$ as a catalyst. Similar results were also obtained for **2** (Fig. 1b). Compound **4** was synthesised using a procedure which has been well practised on the non-labelled version.[2] The specific radioactivities of both **1** (574 KBq mg^{-1}) and **4** (36 KBq mg^{-1}) were more than enough for the current applications, because the concentration of scintillator used is relatively high. When the amount of encapsulated material, such as an enzyme or a co-catalyst, is small the specific radioactivity can be increased accordingly. Further monitoring the ^{3}H NMR spectra of **1** and **2** serves to show that no radiation decomposition occurs at these levels of radioactivity, and the same is true for the [^{3}H]-urethane. The results compare favourably with the corresponding ^{14}C syntheses where much longer times and lower specific radioactivities would be the outcome. The recent development of microwave enhanced tritiation procedures,[13] whereby the tritiation reaction times are reduced to a matter of minutes, widens the gulf between ^{3}H and ^{14}C labelling even further.

The synthesis and properties of the sol–gel glass which encapsulates **1** are similar to those for non-radioactive PPO; repacing ^{1}H by ^{3}H introduces no artefacts. The general sol–gel chemistry for covalently bonding [^{3}H]-4-$HOCH_2$-PPO to the sol–gel matrix, which is also comparable to its non-labelled version, is illustrated in a simplified form in Scheme 3.

The difference between a physically entrapped and covalently bonded sol–gel glass became immediately apparent when leaching test results (Fig. 2) were carried out. In the former more than 85% of the radioactivity had been released over the course of 4 days whilst for the latter the radioactivity appearing in the toluene was hardly above background. Longer term tests—over the course of three months—put the level of leaching at less than 2%.



Scheme 3 Simplified representation of the sol–gel chemistry for covalently bonding **4**.

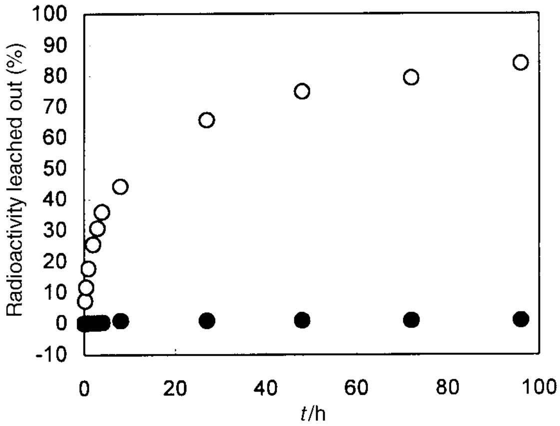


Fig. 2 Radioactivity leaching results for (a) the sol–gel glass physically encapsulating **1** (○) and (b) the sol–gel glass covalently bonding **4** (●).

These very satisfactory results reinforce the fact that leaching is virtually eliminated by covalently bonding PPO into the silica matrix and the sol–gel solid scintillator can be a strong candidate for further applications, *e.g.* detecting a wide range of β^- emitters. The inherent sensitivity of radiation detection using liquid scintillation counting means that these scintillators can be used over a wide concentration range (much more so than using spectroscopic methods). Work to test this hypothesis is currently under way.

Furthermore a radiation detection method, such as liquid scintillation counting, can detect extremely low levels of leaching ($<10^{-10}$ M) in short time intervals. The availability of various labelling methods means that a wide range of organic and biological molecules can be labelled with radioisotopes.[14,15] These features make the widespread application of such radiochemical methods possible. For example, it could be used (a) to detect the leaching in biosensors and bioactive catalysts, (b) to differentiate multi-entrapants by selectively labelling the target, (c) to study the leaching or diffusion mechanism or kinetics in the sol–gel cage.

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