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SYNTHESIS OF 1-(3,4-DIMETHYLPHENYL)-1-[RING-U-^{14}C]PHENYLETHANE, AND OF 1-(3,4-DIMETHYLPHENYL)-1-PHENYL[1-^{14}C]ETHANE, ^{14}C-LABELED DISTILLATE OF ECOSCINT-O^{TM}, A BIODEGRADABLE LIQUID SCINTILLATOR

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SUMMARY

1-(3,4-Dimethylphenyl)-1-[ring-U-^{14}C]phenylethane, and 1-(3,4-dimethylphenyl)-1-phenyl[1-^{14}C]ethane, the ^{14}C-labeled organic solvents of Ecoscint-O^{TM}, a so-called biodegradable scintillation cocktail, were synthesized by simple two-step reactions on a milligram scale. [Ring-U-^{14}C]acetophenone, and [carbonyl-^{14}C]acetophenone were reduced with $NaBH_4$ at the first step, then the resulting 1-[ring-U-^{14}C]phenylethanol, and 1-phenyl[1-^{14}C]ethanol were condensed with *o*-xylene in the presence of H_2SO_4 at the second step. The radiochemical yield of the overall reaction was 16% on a scale starting with 2 mg of acetophenone, and 70% when 50 mg of acetophenone was added as a carrier.

Key words: Biodegradable liquid scintillator, [^{14}C]Ecoscint-O^{TM}, Synthesis

INTRODUCTION

Disposal of radioactive wastes is a serious problem in many countries. Among them, liquid scintillator waste is troublesome to handle because its major constituents are flammable organic solvents containing low level radioactive material. Liquid scintillator waste is normally incinerated, but the work is laborious and expensive. Therefore, a more efficient and safer way of disposal has been desired.

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Various kinds of so-called biodegradable liquid scintillators are now commercially available. They are stated to be less-hazardous, having considerably high flashing points, and easily biodegradable when they are disposed in the sewerage. However, neither the chemical constituents nor the biodegradation mechanism of those scintillator cocktails have been published by the manufacturers.

We examined by means of, for example, GC-MS analysis the chemical constituents of such biodegradable liquid scintillator solvents; they are Ecoscint^{TM}, Eciscint-O^{TM}, Ecoscint-A^{TM} (National Diagnostic Co., USA), and BCS^{TM} (Amersham, England). We found that they are essentially a mixture of monosubstituted benzenes with an alkyl chain of carbon 10 to 13 (Ecoscint and BCS), or 1-(3,4-dimethylphenyl)-1-phenylethane (Ecoscint-O and Ecoscint-A). We also synthesized gram quantities of the organic solvent of Ecoscint-O (and Ecoscint-A) in a good yield (Kurihara and Saito 1990).

We here describe the synthesis of the ^{14}C-labeled organic solvent of Ecoscint-O which will be useful to examine its biodegradable pathway. Fig 1 shows the synthetic pathway.

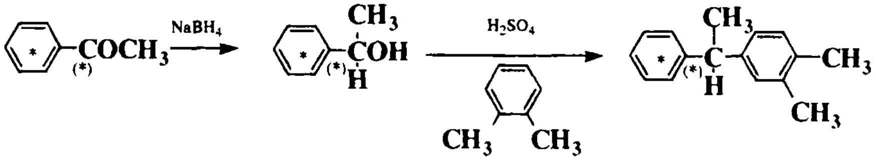


Fig 1. Synthesis of ^{14}C-labeled 1-(3,4-dimethylphenyl)-1-phenylethane. Starting substrates were [ring-U-^{14}C]acetophenone and [carbonyl-^{14}C]acetophenone. ^{14}C-label is indicated by *.

EXPERIMENTAL

Materials and Methods [Ring-U-^{14}C]-, and [carbonyl-^{14}C]-acetophenone (392 GBq/mol, and 370 GBq/mol) were purchased from Sigma Chemicals Co., USA. Purification of synthesized 1-[^{14}C]-phenylethanol and 1-(3,4-dimethylphenyl)-1-[^{14}C]phenylethane was carried out by preparative thin layer chromatography (TLC);

TLC plate: Silica gel 60 F_{254} (200 x 200 mm, 0.25 mm thick, Merck), Solvent system: hexane/acetone (10/1, v/v). The distribution of ^{14}C-radioactivity on the TLC plate was assayed with a Radiochromanizer JTC-501 (Aloka, Japan), a position-sensitive proportional detector. Radiochemical purity of the final product was checked by high performance liquid chromatography (HPLC) with 880-PU (pump, Jasco, Japan), 875-UV (UV-detector, Jasco), and Wakopack $5C_{18}$ (column, 4 mm I.D. x 250 mm, Wako Chemicals, Japan) using a solvent system, acetonitrile/water (4/1, v/v). Flow rate was 1ml/min, and UV-absorption of the HPLC effluent was assayed at 210 nm. The HPLC effluent was collected by fractions and the radioactivity of each fraction was determined with a liquid scintillation counter (LSC) (LKB-Wallac 1219-Rack Beta Spectral, SM, Finland).

Condensation reaction of 1-[^{14}C]phenylethanol with *o*-xylene was carried out by a modification of the larger scale reaction already reported[1].

Reduction of [^{14}C]acetophenone to 1-[^{14}C]phenylethanol

Approximately 7.3 MBq of [ring-U-^{14}C]-, and [carbonyl-^{14}C]acetophenone were transferred into a small test tube with a glass stopper using 2-propanol (0.25 ml x 4). Sodium borohydride (2.5 mgs) was added into a test tube and the mixture was stirred with a magnetic stirrer in a cold room (4 C). After a 48-hrs reaction, 1-phenylethanol (50 μl) was added to the reaction mixture as a carrier only in the [carbonyl-^{14}C]acetophenone experiment. The products were then extracted with diethyl ether (1.5ml x 6) after decomposing any remaining sodium borohydride with dilute hydrochloric acid. The combined ether extracts were dried over Na_2CO_3, concentrated gently *in vacuo* at room temperature, and the solution (c.a. 0.3ml) was applied onto two TLC plates . The main radioactive product which had the same Rf value as authentic 1-phenylethanol was scraped off. Synthesized 1-[^{14}C]-

phenylethanol was extracted from silica gel with 100ml of an organic solvent (with ethyl acetate in [ring-U-^{14}C]acetophenone experiment, and with ethyl ether in [carbonyl-^{14}C]acetophenone experiment). The solvent was then evaporated gently *in vacuo* at room temperature.

Condensation of 1-[^{14}C]phenylethanol with o-xylene *o*-Xylene (0.5 ml) was added to the test tube in which 1-[^{14}C]phenylethanol had been condensed (c.a. 0.2ml). A mixture of conc. H_2SO_4 and fuming H_2SO_4 (3/1, v/v) (70 μl) were added to the test tube with cooling in an ice bath, and the reaction mixture was stirred in a cold room. After 24-hrs reaction, several lumps of ice were added to the test tube, and the resulting mixture was extracted with diethyl ether (1.5ml x 6). The combined ether extracts were dried over Na_2CO_3, evaporated, and analyzed by TLC in the same manner as described above. The major radioactive product which corresponded to the organic solvent of Ecoscint-O was scraped off and extracted with ethyl acetate or diethyl ether in each experiment. The extract was condensed *in vacuo* at room temperature (to c.a. 0.1ml) and transferred into a small glass vial using a small volume of *o*-xylene or methanol.

RESULTS

Reduction of [^{14}C]acetophenone to 1-[^{14}C]phenylethanol The reduced product of [^{14}C]acetophenone showed only one radioactive spot except a trace spot of ^{14}C-substance (1 to 2% of the ^{14}C recovered) at the original position in the radioassay of TLC plate. The main radioactive product had the same Rf value (0.24) as the authentic 1-phenylethanol as shown in Fig. 2. The recovery (%) of 1-[^{14}C]phenylethanol which had been obtained from the TLC plate by extraction with ether was 42% in [ring-U-^{14}C]acetophenone experiment, and 88% in [carbonyl-^{14}C]acetophenone experiment.

Condensation of 1-[^{14}C]phenylethanol with o-xylene After condensation reaction of 1-[^{14}C]phenylethanol with *o*-xylene, very little radioactivity (1 to 3% of the ^{14}C recovered) was observed at the original position of the TLC plate (Fig. 3), showing that the

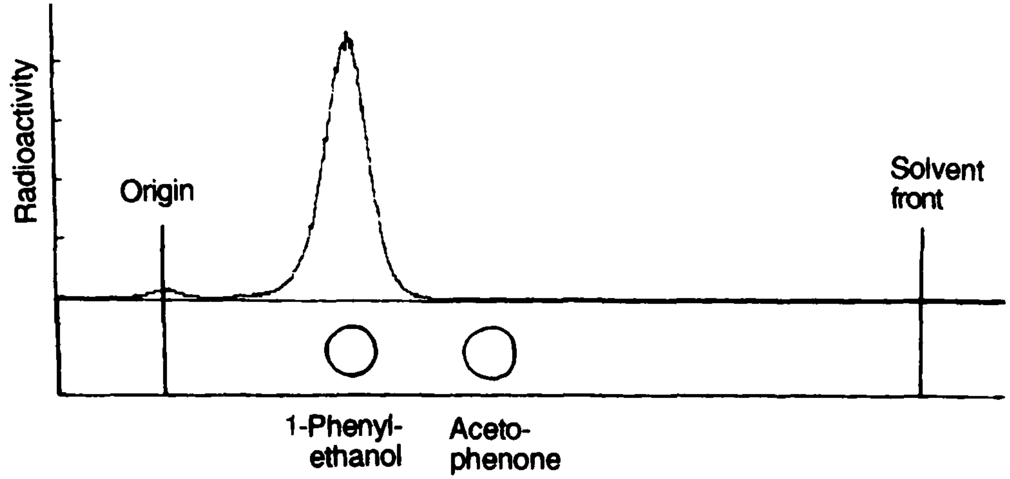


Fig. 2. ^{14}C-distribution of the products synthesized by the reduction of [carbonyl-^{14}C]acetophenone, on the TLC plate. TLC conditions were; Plate: Silica gel 60 F_{254}, 0.25 mm thick, Merck; Solvent: hexane/acetone (10/1, v/v). Circles show the position of each authentic substance visualized by UV-irradiation. (A very similar radiochromatogram was obtained also in [ring-U-^{14}C]acetophenone experiment).

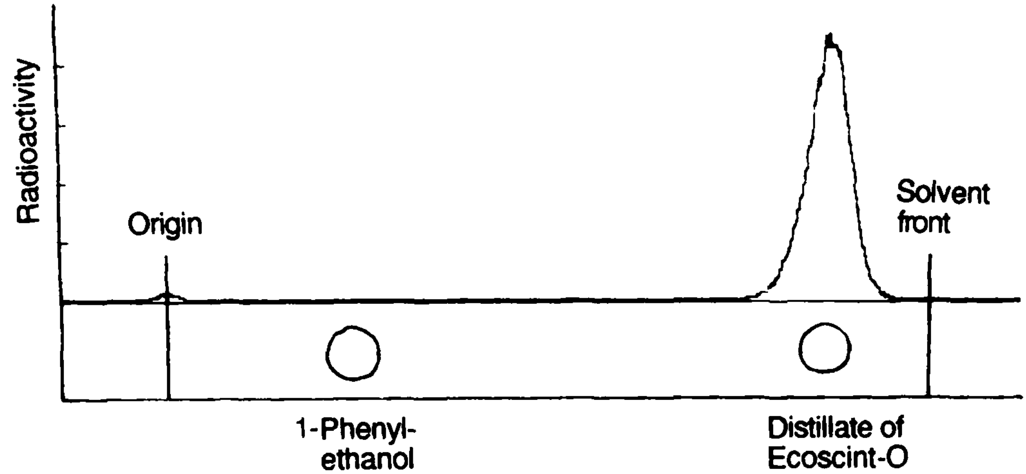
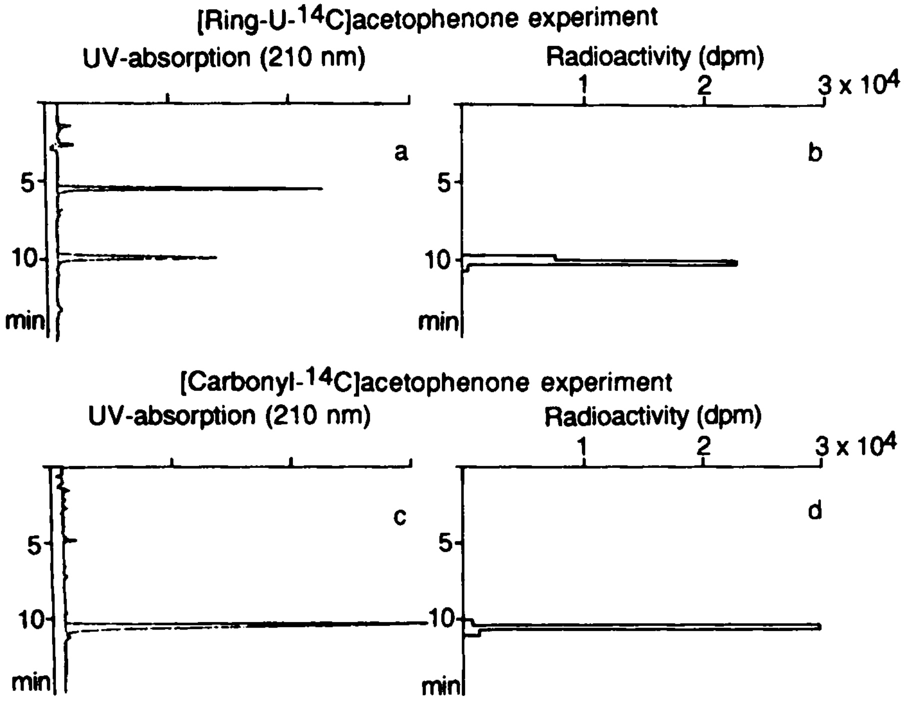


Fig. 3. ^{14}C-distribution of the condensation product of 1-[^{14}C]-phenylethanol with o-xylene on the TLC plate in [ring-U-^{14}C]-acetophenone experiment (TLC conditions were the same as in Fig. 2). Circles show the position of each authentic substance visualized by UV-irradiation. (A very similar radiochromatogram was obtained in [carbonyl-^{14}C]acetophenone experiment.)

condensation reaction also proceeded almost quantitatively. The Rf value of the main ^{14}C-product was 0.87. The radiochemical yield of the TLC-purified final product, the ^{14}C-organic solvent of Ecoscint-O, was 16% in the [ring-U-^{14}C]acetophenone experiment, and 70% in [carbonyl-^{14}C]acetophenone experiment.

Radiochemical purity of synthesized labeled products The ^{14}C-labeled final product, which had the same Rf value as the organic solvent of Ecoscint-O on TLC, was treated by HPLC and the fractions of the effluent were radioassayed by LSC to examine their radiochemical purities. Except the peak of *o*-xylene which was used as a solvent of the final product in the [ring-U-^{14}C]acetophenone experiment, the only one UV-peak which had the same retention time as the distillate of Ecoscint-O was detected in both


[Ring-U-^{14}C]acetophenone experiment

[Carbonyl-^{14}C]acetophenone experiment

Fig. 4. Radiochemical purity of the TLC-purified final product, 1-(3,4-dimethylphenyl)-1-[^{14}C]phenylethane. The labeled substances were analyzed by HPLC using a reverse-phase column, C_{18}, and the mixture of acetonitrile/water (4/1, v/v) as an eluting solvent (flow rate; 1ml/min). The chromatograms (left) were obtained by UV-detection (210 nm), and the radiochromatograms (right) were obtained by counting with LSC the effluent from the column. The ordinate of each chart shows the time duration (min).

experiments (Fig. 4. a, c). Almost all (99%) of the radioactivity injected to HPLC was eluted just accompanying the UV-peak (Fig. 4. b, d), and the radiochemical purity of both samples was 99%, respectively. The specific radioactivity was calculated to be 343 GBq/mol for the ring-labeled final product and 14.7 GBq/mol for the methine-labeled product.

DISCUSSION

The overall radiochemical yields obtained by the [ring-U-^{14}C]acetophenone, and [carbonyl-^{14}C]acetophenone experiments were quite different; i.e. 16% and 70%, but the radiochemical yields obtained by each unit reaction in both experiments were quantitative before concentration of the extract obtained from the TLC plates. The low radiochemical yield observed in the [ring-U-^{14}C]acetophenone experiment is probably due to the vaporization of the ^{14}C-product itself when the solvent, used to extract the ^{14}C-product from silica gel, was evaporated. Therefore, the addition of 50mg of 1-phenylethanol as a carrier, and the usage of ethyl ether that is a low boiling-point solvent as the extraction solvent, were useful to obtain a better radiochemical yield.

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REFERENCE

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