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RADIOACTIVE ALIPHATIC COMPOUNDS

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This invention is a method of producing aliphatic compounds labeled with radioactive carbon-14 atoms.

It is an object of this invention to provide a direct and practical method for producing aliphatic compounds labeled with radioactive carbon-14 atoms.

Another object of this invention is to provide an improved method of producing aliphatic radioactive hydrocarbons useful for tracer studies, particularly in the petroleum industry.

It is a further object of this invention to provide an improved method of producing aliphatic radioactive pharmaceutical compounds useful in tracer studies in the pharmaceutical industry.

The above objects and other objects which will be apparent from the following detailed description are accomplished by this invention which is a method of producing aliphatic compounds labeled with radioactive carbon-14 wherein an intimate mixture of an aliphatic compound and a nitrogen compound is irradiated with thermal neutrons at a high enough neutron flux and for a sufficient time to produce usable quantities of the desired product. An aliphatic compound labeled with radioactive carbon-14 atoms is defined as an aliphatic compound consisting, in part, of molecules having one or more carbon-14 atoms therein. It is preferred to charge a single compound of high purity as the aliphatic component. Likewise the nitrogen compound should be of high purity to prevent contamination of the irradiated product and obtain the highest yields of the desired product. Purities of the order of 99% or higher are preferred but lower purity materials can be used with the result that lower yields will be obtained and it will be more difficult to work up the reaction products to separate the desired compound or compounds. Normally practical yields of labeled aromatic or heterocyclic compounds will not be obtained by the same irradiation techniques due to the complexity of the reactions involved with these compounds.

The aliphatic compounds used as raw materials in this process can be saturated or unsaturated hydrocarbons and substituted hydrocarbons of all kinds including metal esters or soaps, etc. It is preferred to use normally liquid or solid aliphatic compounds in my process since the molecules will be more concentrated and the yields much higher than with gases, unless the gases are under extremely high pressures and substantially as dense as liquids. This method gives particularly high yields of the desired labeled compound when using saturated aliphatic hydrocarbons, particularly normally liquid aliphatic hydrocarbons boiling below about 600° F. Satisfactory yields will be obtained of the desired labeled compound from liquid aliphatic alcohols but these yields will be appreciably lower than from the hydrocarbons.

Nitrogen compounds which can be used as a source as nitrogen-14 in the process can be either inorganic or organic nitrogen compounds. The form of the nitrogen is unimportant due to the nature of the reaction involved.

For the highest yields it is important that the nitrogen compound used be evenly dispersed throughout the aliphatic compound. If a liquid aliphatic compound is being processed normally it is preferred to use a nitrogen compound which is soluble therein since then no problem of intimately dispersing the nitrogen compound in the aliphatic compound is presented. It is preferred that normally liquid or solid nitrogen compounds be used to give a high concentration of nitrogen atoms for irradiation. Gaseous compounds can be used but are not as desirable as the solid and liquid nitrogen compounds except possibly where the gaseous nitrogen compound is very soluble in the particular aliphatic compound being processed. Classes of compounds which are particularly desirable as sources of nitrogen in this process are aromatic and aliphatic amines. About 5 mole percent of nitrogen compound in the mixture of aliphatic compound and nitrogen compound is a satisfactory concentration. This does not necessarily represent an optimum mixture for the highest yield, however, and a higher or lower concentration of the nitrogen compound can be used.

The irradiation is done with thermal neutrons, i. e., neutrons having energies of about 0.03 ev. Suitable sources of these thermal neutrons are nuclear reactors (piles); cyclotrons and the like; radioactive compounds, such as polonium-beryllium sources, etc. The preferred source of thermal neutrons, however, is the nuclear reactor or pile. This source of neutrons will give a high concentration or flux of thermal neutrons for irradiation which will allow the time required in the irradiation step to be substantially reduced as compared to irradiation with a low flux source. A 10^{11} neutrons per cm.^{2} per second source is adequate but a higher flux will allow shorter irradiation time while a lower flux will require more irradiation time to obtain a practical yield of the desired labeled compound.

An irradiation mixture can be worked up by a number of different techniques to separate the desired compound or compounds from the other materials of the reaction mixture. Perhaps the most satisfactory method of working up the reaction mixture is to use a conventional distillation technique wherein carriers are added to facilitate the separation of the minute quantities of radioactive compounds.

Described below are some examples of the use of the process in producing aliphatic compounds labeled with carbon-14. In these examples the total yield of mixed labeled molecules is of the order of microgram quantities.

EXAMPLE I

A 5 mole percent solution of aniline in normal pentane was made. Both materials were 99+% purity. 20 cc. of this solution was inclosed in a quartz tube and irradiated for one week in the heavy water (CP–3′) pile at the Argonne National Laboratory at a flux of 10^{11} neutrons per cm.^{2} per second. Table I shows an analysis of the products of the irradiation step.

EXAMPLE II

20 ccs. of a 5 mole percent solution of ethylamine in normal pentane which was inclosed in a quartz tube was irradiated for one week in the CP–3′ pile at a flux of 10^{11} neutrons per cm.^{2} per second. The irradiated mixture was worked up by the usual distillation techniques using carriers, and the results of the analysis of this mixture are shown in Table II.

EXAMPLE III

A 4.25 mole percent solution of aniline in methanol was irradiated in the same manner as the samples of the other examples and the product worked up by the conven-

tional distillation techniques using carriers. The analysis of the irradiated product is reported in Table III.

Table I.—5 mole percent analine in pentane data

Carrier	Carrier, B. P., ° C.	Boiling Range	Gms. of Sample or Derivative	Absolute DPM× 10^{-4}	Percent of Total Non-Basic Activity
Methane					
Ethane					
Propane					
Butane	−186	−195 to 25	4.5	1.89	12.9
n-Pentane	36	25 to 60	10.7	3.93	26.8
Hexane	68	60 to 95	3.3	2.79	19.0
Heptane	98	95 to 125	3.4	1.20	8.2
Octane	125	125 to 155	4.2	0.74	5.0
Isopropylbenzene	153	155 to 175	4.7	0.83	5.7
Decane	173	175 to 215	4.0	0.76	5.2
Dodecane	215	215 to 245	4.1	0.47	3.2
Tetradecene	246	245 to 290	3.4	0.39	2.6
Heptadecanol	308	290	2.5	1.67	11.4

Table II.—5 mole percent ethylamine in pentane data

Carrier	Carrier, B. P., ° C.	Boiling Range	Gms. of Sample or Derivative	Absolute DPM× 10^{-4}	Percent of Total Non-Basic Activity
Methane					
Ethane					
Propane					
Butane	−186	−195 to 9	4.5	4.62	15
Neopentane	9.5	9 to 25	3.2		0
Isopentane	27	25 to 35	3.1		0
n-Pentane	36	35 to 56	10.0	7.7	25
"Iso" hexane	60	56 to 67	6.5	1.85	6
n-Hexane	68	67 to 95	3.3	4.0	13
Heptane	98	95 to 120	3.4	2.46	8

Table III.—4.25 mole percent analine in methanol data

Carrier	Carrier, B. P. ° C.	Boiling Range	Gms. of Sample of Derivative	Absolute DPM ×10^{-4}	Percent of Total Non-Basic Activity
Methane	−184	−195 to 25	4.8	4.87	38.1
Methanol	65	25 to 72	10.4	2.25	17.6
Ethanol	78	72 to 84	7.9	1.19	9.3
n-Propanol	97	84 to 105	8.0	1.30	10.2
n-Butanol	118	105 to 122	8.1	0.88	6.8
Isoamyl alcohol	130	122 to 150	8.1	0.70	5.5
Higher alcohols	184	150	1.4	1.60	12.5
Aniline (basic cpds)				1.41	

The only significant activity produced in the irradiation of the samples and their containers was the carbon-14 activity.

Table I shows an analysis of the irradiated mixture of Example I. In working up the irradiated mixture the basic compounds such as aniline including basic radioactive compounds were removed by acid extraction. Then carriers were added to the substantially base-free residue from the extraction step and this mixture was distilled. The various fractions from the distillation step were analyzed for absolute activity and reported as disintegrations per minute (DPM). The irradiated mixtures of Examples II and III were worked up in like fashion to that of Example I. Percent of total non-basic activity was calculated from the information on the individual fractions.

The n-pentane fraction of Table I contains 25+% radioactivity and this is almost entirely due to n-pentane labeled with carbon-14. No other fraction carries so much radioactivity. It is indicated that labeling of molecules of the aliphatic hydrocarbon charged to the irradiation step tends to be the predominant reaction.

In Table I analysis data was presented in which the nitrogen for conversion to carbon-14 was furnished by an aromatic amine, aniline. Table II shows data wherein the nitrogen source is an aliphatic amine, namely ethylamine. Complete activity data is not shown in Table II, but it is shown that the activity is highest in the n-pentane fraction and the percentage activity is substantially the same, namely 25%, as when the aromatic amine was used as the source of nitrogen. In other words it is indicated that the source of nitrogen is not critical.

Table III shows analysis data of the irradiated sample from Example III. Aniline was the source of nitrogen and methanol the compound to be labeled. The reason for the highest activity being found in the gas or methane fraction is believed to be the result of carbon-14 atoms replacing oxygen atoms in methanol to form radioactive ethane. Also other radioactive gases including radioactive carbon oxides were probably formed by other reactions. Of the other fractions the greatest activity is in the methanol fraction indicating the production of a substantial and useful amount of the desired radioactive methanol. The yield in radioactive form of the aliphatic alcohol charged to the process would undoubtedly have been appreciably higher had higher alcohol than methanol, such as, ethanol, propanol, butanol, etc., been used due to the nature of the process. The amount of activity found in the basic compounds is shown but not included in the percentage activity calculations.

Obviously many modifications and variations of the invention as hereinbefore set forth may be made without departing from the spirit and scope thereof and therefore only such limitations should be imposed as are indicated in the appended claims.

What is claimed is:

1. A method of labeling aliphatic compounds with radioactive carbon-14 atoms comprising irradiating with thermal neutrons an intimate mixture of a first compound which is a saturated normally-liquid hydrocarbon and a second compound which is a nitrogen-containing compound, the flux of the radiation source being about 10^{11} neutrons per cm.^{2} per second, the mixture containing about 5 mole percent of the second compound in the first compound, and separating the resultant hydrocarbon labeled with radioactive carbon-14 from the irradiated mixture.

2. The method of claim 1 wherein the hydrocarbon is an alcohol.

3. A method of labeling aliphatic compounds with radioactive carbon-14 atoms comprising irradiating in a nuclear reactor an intimate mixture of a first compound which is a saturated normally-liquid hydrocarbon and a second compound which is a nitrogen-containing compound, the flux of the radiation source being about 10^{11} neutrons per cm.^{2} per second, the mixture containing about 5 mole percent of the second compound in the first compound, and separating the resultant hydrocarbon labeled with radioactive carbon-14 from the irradiated mixture.

4. The method of claim 3 wherein the hydrocarbon is an alcohol and the nitrogen-containing compound is an amine which is soluble in said alcohol.

5. A method of producing aliphatic compounds labeled with radioactive carbon-14 atoms comprising irradiating in a nuclear reactor having a flux of about 10^{11} neutrons per cm.^{2} per second an intimate mixture of a major amount of a saturated normally-liquid alcohol and a minor amount of an amine which is soluble in said alcohol, said mixture containing about 5 mole percent of amine in alcohol, and separating the resultant alcohol labeled with radioactive carbon-14 from the irradiated mixture.

6. The method of claim 5 wherein said alcohol is methyl alcohol and said amine is aniline.

7. A method of producing aliphatic compounds labeled with radioactive carbon-14 atoms comprising irradiating in a nuclear reactor having a flux of about 10^{11} neutrons per cm.^{2} per second an intimate mixture of a major amount of a normally-liquid hydrocarbon and a

minor amount of an amine which is soluble in said hydrocarbon, said mixture containing about 5 mole percent of amine in hydrocarbon, and separating the resultant hydrocarbon labeled with radioactive carbon-14 from the irradiated mixture.

8. The method of claim 7 wherein said liquid hydrocarbon is a hydrocarbon boiling below about 600° F.

9. The method of claim 7 wherein said hydrocarbon is pentane and said amine is aniline.

10. The method of claim 7 wherein said hydrocarbon is pentane and said amine is ethylamine.

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