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Comparison of T-recoil and Wilzbach labeling of methylamine (preparation of methylamine-CH_2T)

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Summary

Recoil labeling of methylamine via the $^6Li(n,\alpha)T$*-reaction, using solutions of LiBr in liquid anhydrous methylamine, leads to a 10% radiochemical yield of methylamine-*CH_2T*. The yield is independent of the accompanying radiation dose within a wide range, thus allowing high-dose pile irradiation. Specific activities up to 100 µC/mM can easily be obtained. For comparison Wilzbach labeling of gaseous methylamine has also been studied. Here, in contrast, poor tritium incorporation is observed, the L-value for methylamine-*CH_2T *being* 2.3×10^{-2}.

Introduction

A number of review articles have been published in the past years on the technique of recoil labeling, outlining its advantages and restrictions and some of its applications (1-4). In many cases the major disadvantage of recoil labeling is the concomitant radiolysis taking place during reactor irradiation. Radicals produced by the accompanying ionizing radiation can react with the recoil products formed, thus leading to their conversion into other compounds. Gross radiation damage of the starting material can often be observed after high-dose irradiations. As a consequence the dose applicable and hence the specific activity obtainable is limited.

In the course of our investigation on recoil tritium reactions with simple aliphatic amines (5) we found that the major products are relatively insensitive to radiation dose, the yield of the alkyl group labeled mother compound showing dose independence over a wide range. In case of the methylamine system the relatively high radiochemical yield of the CH_3-group labeled com-

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pound together with the simplicity of the product spectrum seemed to indicate a convenient method for the preparation of methylamine-CH_2T. It was necessary to compare the recoil technique with the Wilzbach labeling of methylamine in order to evaluate the effectiveness of both radiochemical methods and to point out their advantages and limitations.

EXPERIMENTAL

A. *Recoil Labeling*

About 30-40 mg LiBr (Erg. B. 6, Merck) or 10-20 mg LiF (ultra pure, Merck) were placed in quartz ampoules of about 0,3 ml volume. The ampoules were outgassed on a vacuum line to about 10^{-3} mm Hg. By cooling with liquid nitrogen, methylamine gas (Roth) * was condensed from a source bulb into the ampoules, which were then sealed and allowed to warm to room temperature. The ampoules contained about 0,1 ml liquid methylamine. The vapor pressure at 36°C is 5 atmospheres, the solubility of LiBr in liquid methylamine at 20°C is about 520 mg/ml, that of LiF about 10 mg/ml.

The samples were irradiated in the FRJ-1 at thermal neutron fluxes ranging from 10^{11} to 10^{13} n/cm^2sec for either 1 or 10 hours. The temperature was about 30°C, the γ-dose rate at 10^{12} n/cm^2sec about 10^7 r/h. The radiation dose delivered to the sample by the $^6Li(n,\alpha)T$-process was a factor of 5 to 10 greater than that of the external radiation field.

After irradiation the ampoules were stored for a few days to allow decay of the radioactivity from the quartz. The LiBr-containing samples were stored for about two weeks to allow decay of the 36 hour Br-82. The ampoules then were connected to the vacuum line, opened by means of the break seal, and the evaporated sample «toeplered» into a storage bulb. Several aliquots were prepared for radio gaschromatographic analysis and for determination of the total gaseous activity.

B. *Wilzbach Labeling*

For the gas exposure labeling an apparatus was used similar to that described by Wenzel *et al.* (6). Pyrex ampoules of about 85 ml volume (i.d. 30 mm) were filled with methylamine gas to a pressure of 670 mm Hg. After freezing the methylamine with liquid nitrogen, 325 mCi tritium gas was «toeplered» into the ampoules. They were then sealed and allowed to warm to room temperature. After an exposure time of 60 days the ampoules were opened and transferred to a storage bulb for further preparation of aliquots.

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* The gas contained about 1-3 vol % of impurities being mainly dimethyl-and trimethylamine. Using a gaschromatographically purified product did not show any significant change in the results.

C. *Activity Assay and Radio Gaschromatography*

Methylamine gas can be subjected to internal proportional counting without combustion or conversion if its concentration in the counting gas is not too high. Figure 1 shows the effect of methylamine at different concentrations [in a mixture of methane/helium (1:1)] on the plateau of a proportional counter *. It can be seen that below about 10 vol% of methylamine significant plateau shifts do not occur, provided high input sensitivity is applied.

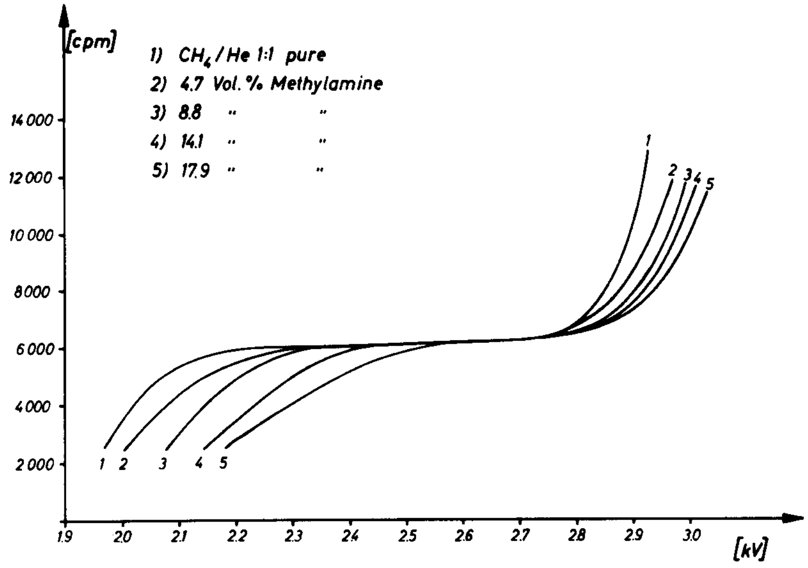

FIG. 1.—Effect of added methylamine on the plateau of a static internal proportional counter.* He/CH4 (1/1) counting gas containing different concentrations of methylamine. External Co-60 source used. 50 ml proportional gas counter FZ 20 P with preamplifier VP 200 TH (input sensitivity 50 mV, preamplification: 200 fold, input sensitivity on detector: 0.25 mV), BERTHOLD, Wildbad, West Germany.

A 10 ml internal proportional flow counter ** was mounted within the gaschromatographic thermostat immediately behind the thermal conductivity detector. Methane was added to the effluent helium carrier gas ($He/CH_4 = 1/1$). The total flow rate passing through the counter was about 100 ml/min. The temperature depending on the GLC-column used (see below) was 20, 30 and 40 °C respectively. The flow counter having a plateau from 2300 to 2700 volts,

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* 50 ml internal proportional counter FZ 20 P with preamplifier VP 200 TH and electronic ESONE equipment from BERTHOLD, Wildbad, West Germany.

** 10 ml internal proportional flow counter LB 6230 from BERTHOLD, Wildbad, West Germany. This counter can be heated up to about 200°C.

was operated at the upper end of the plateau in order to avoid poisoning effects of the methylamine passing through the sensitive volume (see also fig. 1).

Samples of about 1-2 ml (NTP) were generally injected. Registration of the radioactivity was carried out by means of a digital printout system. (7)

The following gaschromatographic columns were used:

1) For the separation of HT and CH_3T: 2 m aluminum column, 4 mm i.d., filled with activated charcoal, 35-40 mesh, 20 °C, 48 ml He/min.
2) For the separation of ammonia, trimethylamine, methylamine, dimethylamine and ethylamine: 3 m steel column, 4 mm i.d., filled with 30% w/w *o*-toluidine on chromosorb W, 60-80 mesh 30 °C, 45 ml He/min.

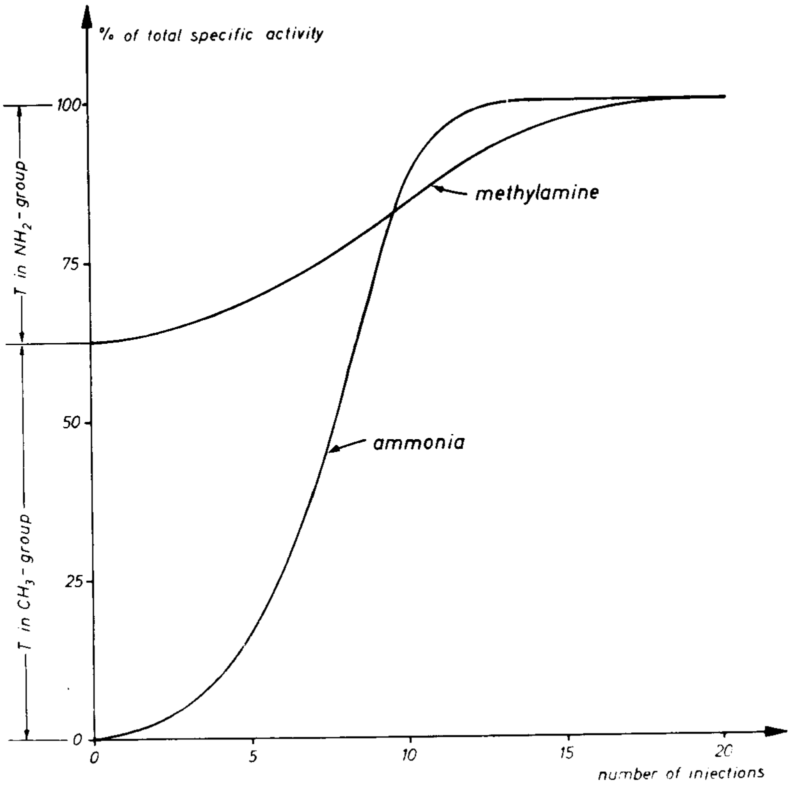

FIG. 2. — Determination of labile tritium by the equilibrium exchange method on a gaschromatographic column.

% of total specific activity versus number of injections. 1 ml (NTP) samples of T-ammonia or methylamine-CH_2TNHT injected. 4,5 m column, 4 mm i.d., filled with 20% w/w of DMS on teflon, 40-60 mesh, 30°C, 60 ml He/min.

A complete exchange of labile tritium takes place on the *o*-toluidine column. Tritium in N-H bonds can thus readily be removed, so that only the activity of the C-H bond labeled products is measured. Since the amount of *o*-toluidine and hence the number of N-H bonds is very large compared to the amount of the labeled amine injected, complete removal of labile tritium is effective for a great number of injections. The labile tritium from the column can finally be removed by injections of large amounts of inactive methylamine. The method of exchanging labile tritium on gaschromatographic columns had been applied for labeling purposes by Elias *et al.* (8) Exchange of tritium from N-H bonds of amines takes place on practically every GLC-column, partly also on the solid support and the walls of columns and vessels. Even if teflon is used coated with such stationary phases as dimethylsulfolane or Kel-F, a complete loss of labile tritium is observed in the first few injections of small samples. However, saturation can easily be obtained. Using this equilibrium method on an «inert» column, the total labile tritium can be determined.

Figure 2 shows two typical curves which were obtained with the equilibrium method for labile tritium from ammonia-T and from methylamine, respectively, the latter labeled in both the CH_3- and the NH_2-group. The specific activity of the NH_2-group is given by substracting the specific activity after the first injection from that appearing after saturation (see fig. 2). For this experiment the following column was used: 3) 4,5 m aluminum column, 4 mm i.d., filled with 20% w/w of dimethylsulfolane on teflon, 40-60 mesh, 60 ml He/min, 30 °C.

1 ml samples of ammonia or methylamine with a specific activity of about 10,000 dpm/ml V(NTP) were injected.

It should be pointed out, however, that no information can be obtained on the primary yield of labile tritium containing compounds formed in small amounts or carrier-free in methylamine, since they will exchange with N-H bonds of the excess methylamine. In this case practically the total labile tritium will appear in the NH_2-group of the labeled methylamine.

RESULTS AND DISCUSSION

A. *Recoil Labeling*

The major products resulting from the $^6Li(n,\alpha)T$-reaction in liquid methylamine are HT, CH_2TNH_2 and CH_3T. They represent about 85 to 98% of the total induced activity, depending on the radiation dose. The rest are labile tritium containing products, predominantly NH_2-group labeled methylamine. Since the recoil spectrum is generally strongly affected by the dose of the accompanying ionizing radiation, we have varied the dose by about a factor of 100, corresponding to an nvt of about 4×10^{14} to 4×10^{16} n/cm^2. The dose dependence of the product yields is shown in figure 3. We have plotted the radiochemical yield in % of the total induced activity versus the dose in eV/molecule, delivered to the system by the $^6Li(n,\alpha)T$-process (Q = 4,78 MeV). This dose was derived from the experimentally determined total tritium activity. In the above mentioned experiments (about 35-40 mg of natural Li-containing LiBr were dissolved in about 0,1 ml liquid methylamine) the dose from the nuclear process exceeds that of the external pile irradiation by a factor of 7-8.

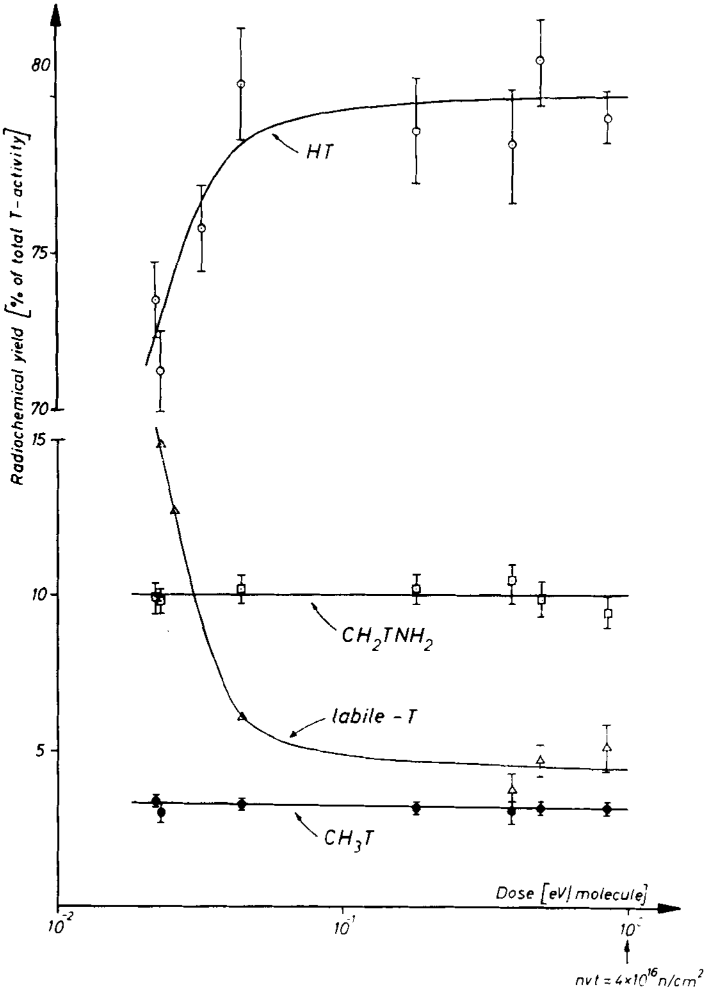

FIG. 3. — Dose dependence of the recoil products in liquid methylamine. Yields in % of total induced T-activity versus dose in eV/molecule.

It can be seen from figure 3 that the yield of HT increases with increasing dose from about 73% to a saturation value of about 80%. A concomitant decrease of the yield of the labile tritium containing products is observed. This effect is clearly due to exchange reactions between tritium from N-H bonds and radiolytically produced hydrogen.

The yield of CH_3T and that of the CH_3-group labeled methylamine, however, remains constant within the dose range studied. It is interesting to note that the radiation insensitivity of these products is also reflected by the complete lack of scavenger effects in this system. The addition of 1 mole% of propylene or iodine as scavenger does not change the product yield. The self-scavenging properties of amines and the mechanistic aspects of product formation will be discussed elsewhere (5).

The dose independence of the 10% radiochemical yield of CH_3-group labeled methylamine together with the simplicity of the product spectrum suggests a simple labeling method. In addition, the relatively good solubility of LiBr in liquid methylamine allows one to use a homogeneous system. The specific activity of the CH_3-group labeled amine that can be obtained with a saturated solution of LiBr in liquid methylamine after a 1 hour irradiation at a flux of 10^{13} n/cm^2sec is about 20 μCi/mM. It can be increased by a factor of 13.5 when Li-6 is used. In praxi specific activities of 100-200 μCi/mM could easily be reached. The production of C-14 labeled compounds via the $^{14}N(n, p)^{14}C$-process can be neglected, especially since the radiochemical yield of C-14 labeled methylamine in liquid methylamine is only about 2% (9). Thus, taking into account the half life and the activation cross section, the specific activity of the C-14 labeled product would be smaller by a factor of about 10^4.

Large amounts of T-labeled amine can readily be produced. After irradiation and a proper storage time, necessary to allow a safe handling of the ampoules, a radiochemically pure product is obtained by passing the irradiated samples through an *o*-toluidine column. This purification will ensure removal of labile tritium from the NH_2-group as has been described above.

B. *Wilzbach Labeling*

Wilzbach labeling of methylamine was carried out in the gas phase since the gas exposure method is generally most effective in a homogeneous gaseous system. In recoil labeling, however, higher radiochemical yields of methylamine are observed in the liquid than in the gas phase (in the latter case using the $^3He(n, p)T$-process) (5). In table 1 the results of a 19.5 Curie-day (0.325 Ci for 60 days) gas exposure experiment is compared with those from recoil labeling. Yields are given in % of the total induced activity for the recoil experiment and in % of the total tritium activity applied, for the exposure experiment. In addition, the L-values (number of labeled molecules produced per average decay energy of tritium = 5700 eV) are also listed.

It can be seen that only poor tritium incorporation is obtained by the gas exposure method, the L-value for the formation of the CH_3-group labeled methylamine being 2.3×10^{-2}. L-values generally increase with increasing concentration of T_2, due to the increased dose rate of β^--radiolysis and hence a larger contribution of radiation chemical reactions (10-13). But the proportion of tritium found in by-products also increases (14). In the case of the methylamine system, however, it seems unlikely that the formation of the CH_3-group labeled amine would be strongly favored. The major products from radiation induced reactions would be CH_3T and NH_2T resulting from a reductive fission of the C-N bond in methylamine (15). This is also expressed by the relatively high L-value for CH_3T (0.46). Labeled ammonia cannot be found since it would exchange with N-H bonds of the excess methylamine.

TABLE 1. Comparison of T-Recoil and Wilzbach Labeling of Methylamine.

Product	Recoil * [% of total activity]	Gas exposure ** [% of total activity]	[L-value]
HT (+T_2 resp.)	78.5 ± 1.2	99.5	
CH_3T	3.1 ± 0.1	0.45	4.6 × 10^{-1}
CH_2TNH_2	10.8 ± 0.9	0.022	2.25 × 10^{-2}
labile T	7.6 ± 0.5	0.038	3.92 × 10^{-2}
$(CH_2T)N(CH_3)_2$	—	0.002	2.6 × 10^{-3}
$(CH_2T)NH(CH_3)$	—	0.009	9.4 × 10^{-3}
C_2H-TNH_2	—	0.002	2.6 × 10^{-3}

* 35 mg LiBr dissolved in 0.1 ml liquid methylamine, irradiated at a thermal neutron flux of 10^{12} *n*/cm^{2}sec, 1 h, radiation dose about 10^{-1} eV/molecule.

** Gas phase, 670 mm Hg, 325 mCi T_2, 60 days.

CONCLUSION

In the above mentioned Wilzbach gas exposure experiment the specific activity of the methylamine-CH_2T is 23 μCi/mM. It can be increased by using larger amounts of T_2. Thus, the specific activity can in principally be made higher by Wilzbach labeling than by recoil labeling. The actual man hours used in both experiments are about the same. However, the yield of CH_2TNH_2 in % of the total tritium produced or applied, is considerably higher (about a factor of 490) in recoil labeling. In the gas exposure experiment a larger amount of T_2 is «wasted», since most of it appears as HT (due to the exchange reaction with radiolytically produced hydrogen during exposure) and can no longer effectively be used for Wilzbach labeling. The recoil method is more economical. In addition, the low L-values obtained in gas exposure require long exposure times. This leads to the conclusion that the preparation of CH_3-group labeled methylamine can more conveniently be carried out by the recoil technique than by the Wilzbach method when specific activities of some 10 μCi/mM are required. Li-6 has to be used if some 100 μCi/mM have to be produced. An increase of the neutron dose does not bring any further advantage, because of the production of the C-14 labeled product (see above). The gas exposure method hence is superior in the range of 100 µCi/mM to mCi/mM. Finally, classical synthesis will be necessary to prepare a product with specific activities of some 10-100 mCi/mM.

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