RECOIL SYNTHESIS OF

HIGH SPECIFIC ACTIVITY ^{11}C-CYANIDE

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ABSTRACT

The low radiation dose associated with the short half life of ^{11}C (20.4 min), the good spatial resolution possible in imaging β^+ emission and the near identity of ^{11}C containing compounds to their ^{12}C homologues, make ^{11}C labeled organic compounds very attractive for use in Nuclear Medicine. As an initial step in the synthesis of ^{11}C amines and amino acids we have developed methods for direct recoil synthesis of large quantities of $^{11}CN^-$. We used the $^{14}N(p,\alpha)^{11}C$ reaction with bombardment of solid $LiNH_2$ or a gas target containing 99% N_2 and 1% H_2. Using a continuous flow of N_2+H_2 through a quartz-lined gas target we have routinely recovered in the gas flow from the target over 500 mCi of $^{11}CN^-$ following bombardment with 15-30 μA of 15 MeV protons for 30 to 45 minutes. Analysis of all of the ^{11}C activity in the gas stream from the target during bombardment showed ~61% $H^{11}CN$, ~28% ^{11}C hydrocarbons, ~9% Co and ~2% CO_2. The total $H^{11}CN$ recovered amounted to ~20% of the total theoretical yield in the target.

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INTRODUCTION

Carbon-11 is potentially the most useful label for the study of in vivo distribution and metabolic fate of organic compounds because of its decay characteristics and its ability to substitute for stable C-12 without significantly influencing the chemical behavior of the organic compound[1,2]. Carbon-11 has a t 1/2 of 20.4 min decaying by positron emission directly to the ground state of the stable ^{11}B daughter, thus providing a low radiation dose radioindicator well suited to high resolution positron scintiphotography.

Among the nuclear reactions by which ^{11}C activity may be induced, the following are most useful for the production of high specific activity radioindicators:

$$^{10}B(d,n)\ ^{11}C \qquad (1)$$

$$^{11}B(p,n)\ ^{11}C \qquad (2)$$

$$^{14}N(p,\alpha)\ ^{11}C \qquad (3)$$
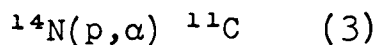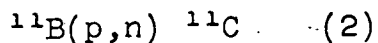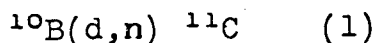
Reactions (1) and (2) have been used in our laboratory for the production of a number of ^{11}C labeled carboxylic acids by recoil synthesis of ^{11}CO in targets of B_2O_3 and subsequent oxidation to ^{11}CO$_2$ followed by incorporation of the ^{11}CO$_2$ into organic acids using Grignard or Aryl-lithium reagents[3,4].

Other types of labeled organic compounds can be synthesized through use of ^{11}C-labeled cyanide ion. For example, amines can be prepared by reduction of cyanohydrins resulting from reactions of $(^{11}CN)^-$ with a variety of aldehydes and ketones, and amino acids can be prepared by hydrolysis of aminonitriles (Strecker synthesis).

Following recommendations arising from the work of Wolf and Finn

at the Brookhaven National Laboratory (personal communication) we have developed recoil syntheses of ^{11}C-cyanide with high specific activity using two different target systems. One is a solid batch process, while the other employs a gas target which may be operated with continuous flow. Both are based upon the ^{14}N(p,α) ^{11}C reaction.

^{14}N(p,α) ^{11}C

This nuclear reaction has been studied by Nozaki, et al[5], who have measured the excitation function up to proton energies of about 15 MeV. The cross-section maximum, occurring at about 7.5 MeV, is over 175 mb. Graphical integration of their data indicates an average cross section, over the proton energy interval 4-15 MeV, of about 75 mb. The theoretical thick target activation yield obtainable during an irradiation of 1-half life duration (20.4 min) is about 1 curie for 15 µA of 15 MeV protons incident on a pure nitrogen target. The target thickness used in the calculation was obtained from Figure 1.

Lithium Amide Target

For the batch production of ^{11}C-cyanide having high specific activity, a lithium amide powder target is suitable. This compound was chosen because proton induced ^{11}C "hot atoms" recoiling into the sample matrix could theoretically form C-N bonds, subsequently producing Li ^{11}CN from which carrier-free H^{11}CN is easily recovered. Competing reactions include formation of ^{11}C-hydrocarbons from recoil reactions with LiNH$_2$ and ^{11}C-oxides from reactions with oxygen impurities in the target. Based upon the range energy curve shown in Figure 1, the theoretical ^{11}C yield following a 20-min bombardment with

15 μA, 15 MeV protons is about 0.5 curie.

A sample of lithium amide (Alpha Inorganics), sufficiently
thick to stop the incident beam, was bombarded for 20 min with 15 μA,
15 MeV protons at the Berkeley 88-inch cyclotron. The water-cooled
high level target assembly is shown in Figure 2. The irradiated sam-
ple, which appeared undamaged by the ion beam, was dissolved in 15
ml of H_2O containing 10 mg KCN as carrier and 10 mg K_2CO_3 as scaven-
ger for ^{11}C oxides. Ammonia, produced by $LiNH_2$ hydrolysis, was re-
moved by boiling, the carbonates removed by precipitation with
$Ba(OH)_2$, and the filtrate transferred to a distilling flask. Ten ml
9N H_2SO_4 were added and the HCN distilled into an ice-cold H_2O trap.
The chemical recovery was determined by argentometric titration of
an aliquot of the trap solution, and the remainder was treated with
excess $AgNO_3$, acidified with HAc. The AgCN precipitate was washed,
redissolved in NH_4OH, and radioassayed. The yield of $H^{11}CN$, re-
ferred to end of bombardment, was 18 mCi. The KCN carrier addition
may be omitted for production of high specific activity $H^{11}CN$. This
yield represents 3.6% of the theoretical ^{11}C production.

Nitrogen-Hydrogen Gas Target

A target system from which the induced activity can be recovered
in good yield in the gas phase offers several advantages. Most im-
portant is that chemical treatment can proceed simultaneously with
radioactivation through continuous recovery of the active gasses.
The result is reduced post irradiation processing time and, therefore,
less activity loss through radioactive decay. Recovery of the product
in the gas phase also reduces contamination because non-volatile ac-
tivities remain in the target chamber. A third advantage is the ease

of monitoring the progress of an irradiation by surveying the flow of radioactivated gasses.

The reactions of recoiling atomic ^{11}C and ^{11}CN radicals, and the recoil synthesis of ^{11}C compounds in various gas systems have been studied by a number of workers[6,7,8,9]. These data suggest that a proton irradiation of a nitrogen gas target containing a small amount of hydrogen (1-5%) might result in production of large quantities of $H^{11}CN$, recoverable continuously in the gas phase. The observed reaction products include $H^{11}CN$, ^{11}CO, $^{11}CO_2$ and $^{11}CH_4$. The ^{11}C-oxides result from chemical combination of recoiling ^{11}C with trace oxygen impurities in the systems.

Our continuous flow gas target, shown in Figure 3, consists of a 100 cm x 2-in (diam) stainless steel pipe fitted with a front flange and 1"-diam collimator-window assembly. The foil window is cut from 0.001-in thick Havar[10]. At the downstream end of the target pipe is the gas outlet, controlled by a remotely operated needle valve, to which is connected a teflon delivery tube terminated by a 10-20 μ sintered glass gas diffuser. The target-gas inlet system is located near the front flange. Shown in the foreground of the figure is the quartz target liner which is inserted into the target pipe and sealed in place with o-rings. A gas inlet hole, blown into the quartz tube wall, is positioned beneath the target gas inlet. The $H^{11}CN$ trap assembly consists of a Lucite water bath surrounding and supporting a 30 ml syringe barrel which is connected to a remotely operated solenoid valve.

In preliminary experiments, using target pipes made of aluminum, brass, gold plated brass, and stainless steel (all without the quartz

liner) we were able to obtain satisfactory yields of ^{11}C-cyanide, though not recoverable in the gas phase. Dubrin, et al[7], noted a similar difficulty in their recoil reaction studies, concluding that the H[11]CN in trace quantities was complexed to the metal target walls. Asche, et al[8], however, were able to recover a large fraction of H[11]CN from their glass target vessel. With the quartz liner we were able to prevent significant loss by incomplete recovery in the gas phase.

High purity (99.999%) nitrogen gas containing 1.0% hydrogen was introduced into the target to maintain an internal pressure of 60 lb/sq.in. The outlet needle valve was adjusted to produce a satisfactory bubble rate in the diffuser-trap. The gas flow rate was about 0.5-0.75 l/min. The target pipe was wound with a 12 ft. insulated heating tape and heated to an external wall temperature of 200°C. During bombardment with 30 μA of 15 MeV protons, the external heater was turned off, and the power deposited by the beam was allowed to maintain the target wall temperature at about 200-250°C.

The activated gasses from a 45-min bombardment were bubbled through an ice-cold H_2O trap containing KCN and K_2CO_3 carriers which absorbed H[11]CN and [11]CO_2 from the gas stream. The remaining active gasses were passed through a Drierite® column into a gas collection bag. After the end of bombardment the trap was analyzed for ([11]CN)[-] and ([11]CO_3)[=] and the remaining gas aliquoted from the bag for [11]CO and ^{11}C-hydrocarbon assay. The [11]CO was separated by passing a sample of the gas, mixed with air, through a column of active Hopcalite® and then trapping the product [11]CO_2 in a dilute alkali trap. A second sample of the gas was passed through a column of CuO at 900°C into an alkali trap. This treatment oxidized both [11]CO and

^{11}C-hydrocarbons to $^{11}CO_2$. The ^{11}C-hydrocarbon yield was then determined by difference of the radioassayed gas aliquots. The composition of the activated gas was found to be 61.3% $H^{11}CN$, 27.7% ^{11}C-hydrocarbons, 9.1% ^{11}CO, and 1.9% $^{11}CO_2$. The $H^{11}CN$ activity yield was 673 mc, almost 20% of the theoretical ^{11}C yield.

ACKNOWLEDGMENT

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FIGURE CAPTIONS

Figure 1   Theoretical ranges[11] of protons in Lithium Amide
and Nitrogen as a function of Proton energy.

Figure 2   88-inch cyclotron High Level Target Assembly.

Figure 3   Quartz lined continuous flow gas target.
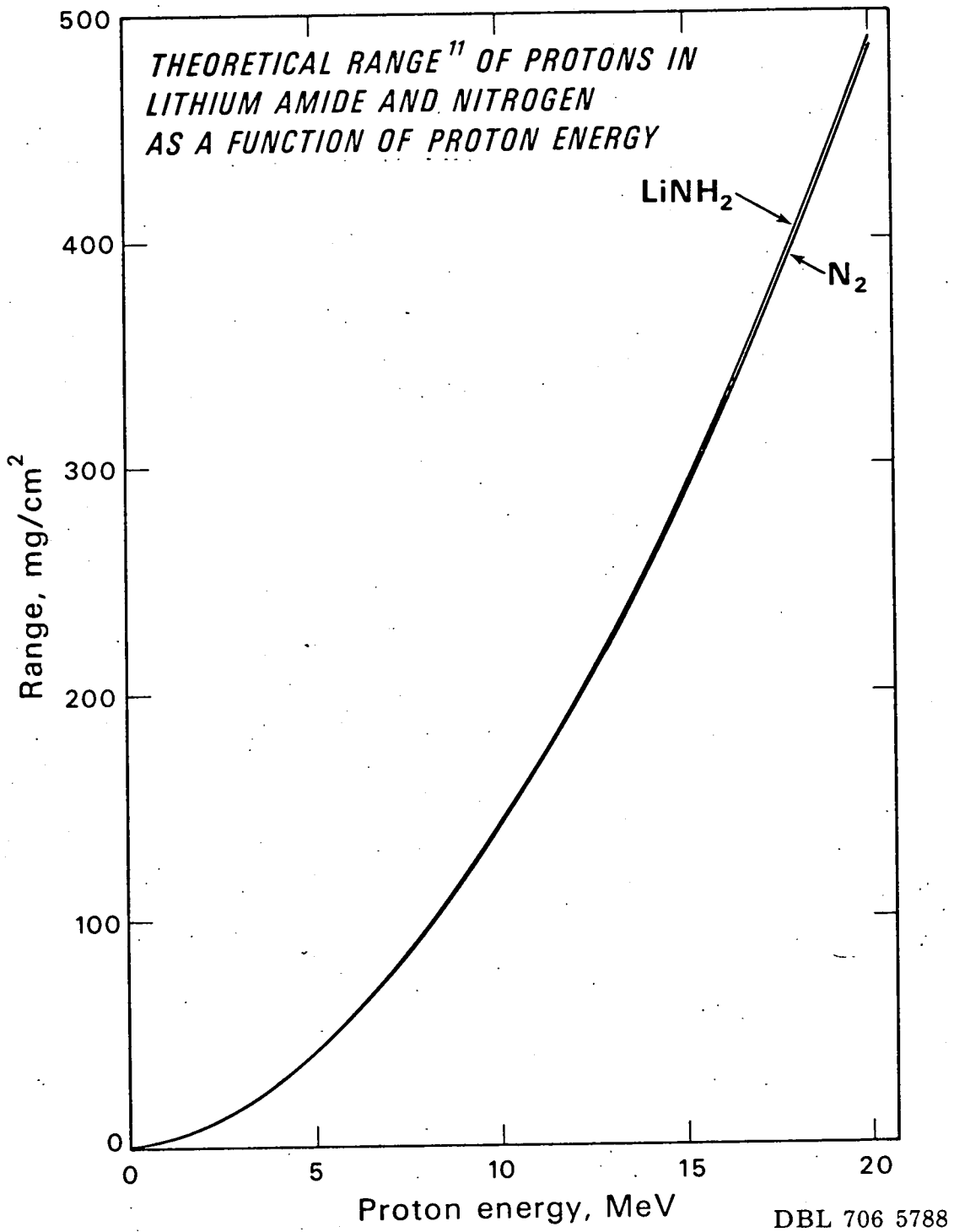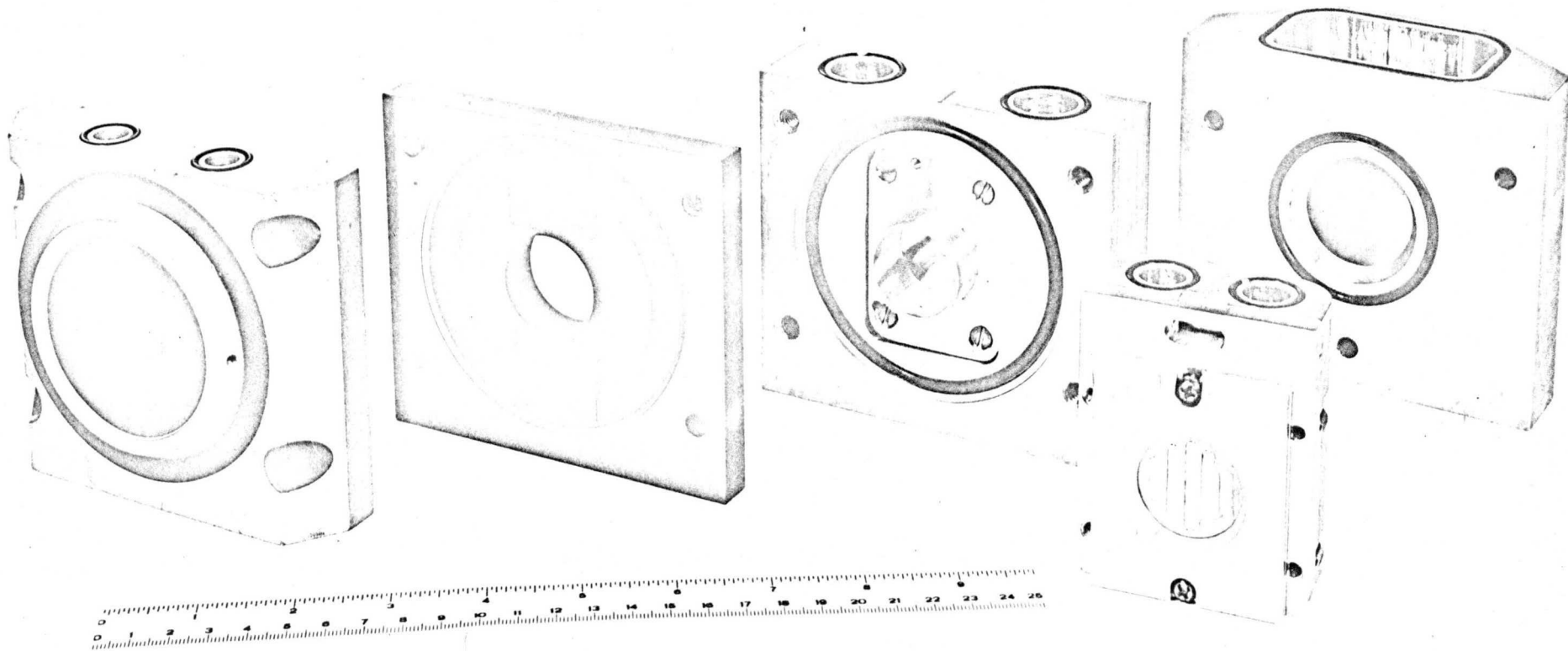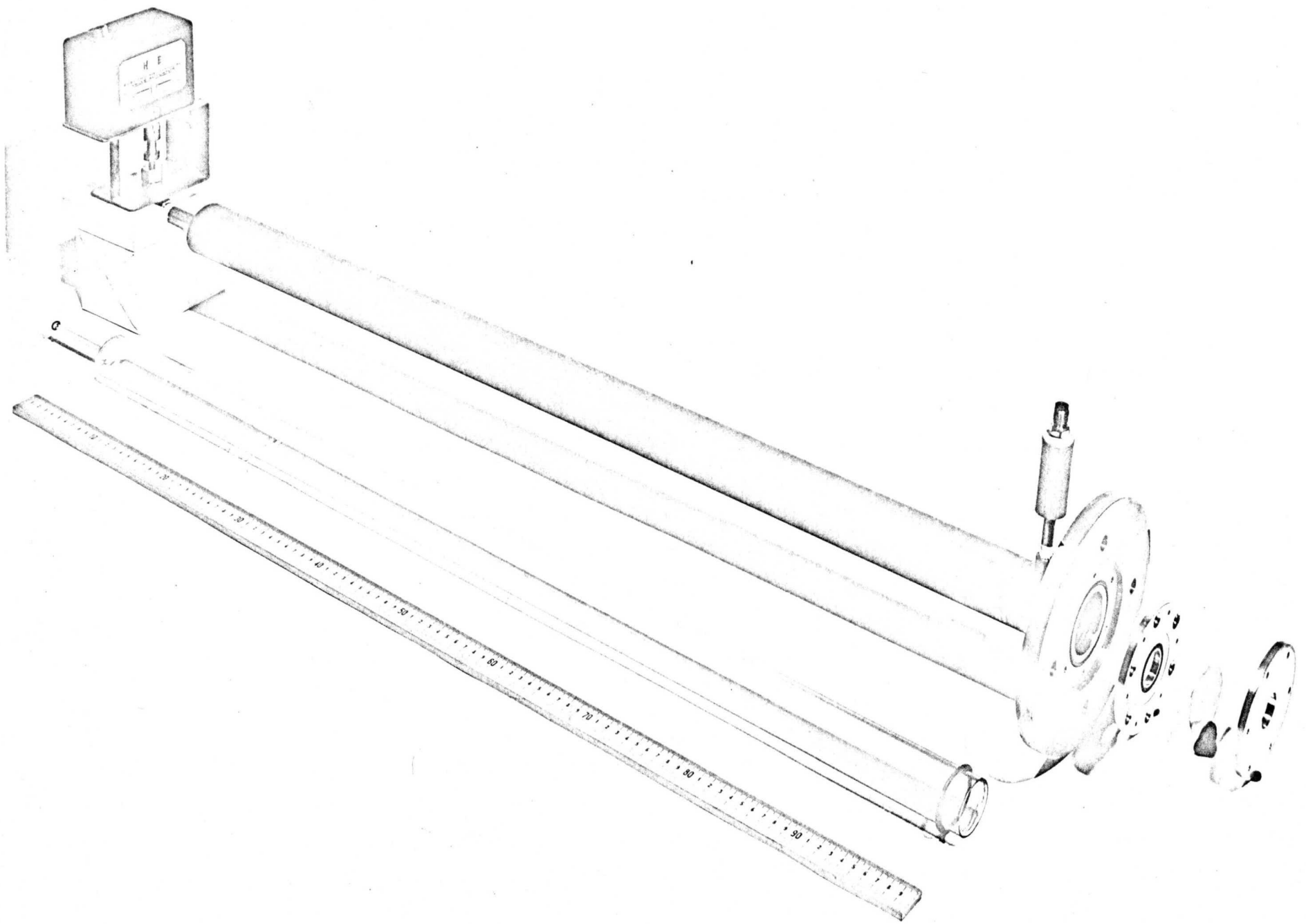
THEORETICAL RANGE[11] OF PROTONS IN LITHIUM AMIDE AND NITROGEN AS A FUNCTION OF PROTON ENERGY

Figure 1

Figure 2

Figure 3