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RTI/2227/00-09 Date: May 1985

Project Report No. 9

ADSORPTION, DISPOSITION, METABOLISM AND EXCRETION OF CROTONALDEHYDE

Dates of Study: July 1983 to August 1984

Contract No. NO1-ES-1-5007
Pharmacokinetics of Xenobiotics

Submitted to:

National Institute of Environmental
Health Sciences
P. O. Box 12874
Research Triangle Park, NC 27709

Prepared by:

[redacted]
Assistant Director for
Bioorganic Chemistry
Chemistry and Life Sciences

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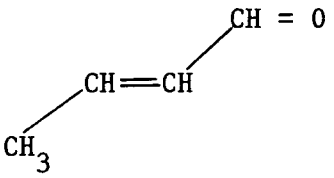
ADSORPTION, DISPOSITION, METABOLISM AND EXCRETION OF CROTONALDEHYDE IN MALE F344 RATS



Abstract

[^{14}C]Crotonaldehyde of greater than 96% radiochemical purity was obtained as a 1:9 ethanol:water solution by high performance liquid chromatography of commercial [^{14}C]crotonaldehyde. When [^{14}C]crotonaldehyde was incubated at a concentration of 300 μg/mL with a 20% suspension of stomach contents in normal saline for 2 h at 37°C, 94% was recovered unchanged and another 5% was bound to particulate material. In plasma, 42% of a 7 μg/mL solution of [^{14}C]crotonaldehyde was recovered intact after 5 min at 37°C; 15% after 30 min.

After intravenous administration of ca. 3 mg/kg, [^{14}C]crotonaldehyde was rapidly metabolized and excreted. Within 6 h of dosing, 31% of the dose was excreted as $^{14}CO_2$ in breath and 37% as unknown metabolites in urine. After 72 h, approximately half of the dose had been excreted in urine and 40% in breath. Elimination of ^{14}C by breath and urine was (at least) biphasic, with similar half lives of ca. 2 and 13 h calculated for each route. Parent compound accounted for less than 1% of the urinary excretion of ^{14}C and crotonic acid for less than 2 percent.

Less than 1% of the dose was excreted in feces. There was no significant accumulation of ^{14}C in any tissue. Blood and major tissues

exhibited rapid initial elimination of ^{14}C, with half-lives of ca 1 h followed by much slower elimination of the remaining ^{14}C with half-lives of 2.5 days or greater. It would not be unexpected for the slowly eliminated ^{14}C to be products of the reaction of crotonaldehyde and bio-molecules.

Orally administered [^{14}C]crotonaldehyde at doses of 0.7, 3 and 35 mg/kg was greater than 90% absorbed. Within 12 h of dosing, 78, 74 and 60 percent of the dose, respectively, had been excreted in breath and urine. In 3 days, 86, 83 and 82%, respectively, had been excreted by these routes. An additional 7% of the dose was excreted in feces.

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List of Participants

Study Director

Veterinarian

Chemist

Chemist

Chemist

Animal Technician

1.0 Introduction

Crotonaldehyde, 2-butenal, is an intermediate in the manufacture of crotonic and sorbic acids, n-butanol, n-butyraldehyde, resins, and rubber antioxidants. It is also used as a warning agent in fuel gases. Crotonaldehyde is an irritant of the eyes, mucous membranes and skin. Since this aldehyde is found in drinking water, cigarette smoke, and possibly smog, it is considered to have considerable potential for human exposure. Crotonaldehyde is a clear liquid that is soluble in water, THF, acetone, and ether but only slightly soluble in ethanol.

Crotonaldehyde is known to react rapidly with thiols, including glutathione (Boyland and Chasseand, 1967; Gray and Barnsley, 1971). The reaction with glutathione was reported to yield at least two major products. Two metabolites have been identified from rat urine as 3-hydroxy-1-methylpropylmercapturic acid and 2-carboxy-1-methylethyl-mercapturic acid (Gray and Barnsley, 1971).

2.0 Materials and Methods

2.1 Animals

Source: Adult male Fischer 344 (F344-M) rats were purchased from Charles River Breeders (Kingston, NY). The rats were examined for signs of disease or abnormality upon arrival and quarantined at least two weeks before they were used in a study. Animal weights at the time they were in studies are shown in Table 1.

Diet: Animals were fed Certified Purina Rat Chow and furnished water ad libitum. Prior to the oral dosing experiments, animals were fasted overnight.

Housing: Animals were transferred to individual glass metabolism chambers the day before they were used in an experiment. These chambers provided for separate collection of urine and feces and for trapping of ^{14}C in exhaled breath. Animals which were sacrificed $\leq$6 hr after dosing were housed singly in polypropylene cages.

2.2 Xenobiotic

The ^{14}C labeled test compound, crotonaldehyde, was supplied by NIEHS. It had been prepared by Midwest Research Institute, Lot No. 83-127-16-30 and was supplied as an aqueous solution containing 4.74 mCi of [^{14}C]crotonaldehyde. The stated concentration was 3.64 mCi/mL (1.58 mM/mL, 11% w/v), with a specific activity of 2.31 mCi/mmole. A copy of the data sheets is included as Figure A1 in the Appendix of this report. Unlabeled crotonaldehyde was obtained from Aldrich Chemical Company, Lot No. 1217PH, as an aqueous solution. Although Aldrich reports this to be a solution of 85% crotonaldehyde and 15% water, actual values were found to be 93% crotonaldehyde and 7% water by Karl Fischer water determination. The radiochemical purity of the [^{14}C]crotonaldehyde was

established by high performance liquid chromatography (HPLC) on a Waters Associates liquid chromatograph equipped with two Model 6000A pumps, a Model 720 solvent programmer, a Model U6K injector and a Model 773 Spectroflow (Kratos) ultraviolet detector operated at 223 nm. The HPLC column was a Du Pont Zorbax ODS (0.46 x 25 cm) and the mobile phase consisted of mixtures of acetonitrile and water. A linear solvent gradient was run from 20:80 acetonitrile:water to 95:5 acetonitrile: water over 10 min. The mobile phase flow rate was 1.5 mL/min. Unlabeled crotonaldehyde, 1 μg/μL in water, and [^{14}C]crotonaldehyde, 4.06 x 10^2 DPM/μL water, were chromatographed. Following the injection of [^{14}C]crotonaldehyde, column effluent was collected in fractions and the ^{14}C eluting in each fraction was measured by liquid scintillation spectrometry. The radiochemical purity of the [^{14}C]crotonaldehyde was ca. 83% (Figure 1). Unlabeled crotonaldehyde appeared essentially pure by HPLC analysis (Figure 2).

2.3 Preparation of Dose Forms

Purification of [^{14}C]Crotonaldehyde. Before dose preparation, the [^{14}C]crotonaldehyde was purified by HPLC. A Du Pont Zorbax ODS (0.46 x 25 cm) HPLC column with a Bondapak Corasil C_{18} pre-column was employed. The mobile phase was a 10% (v/v) mixture of ethanol in water at a flow rate of 1.5 mL/min. After an injection of ca. 0.7 mg of impure [^{14}C]crotonaldehyde was made, the fraction eluting from the HPLC column which contained [^{14}C]crotonaldehyde was collected in an argon purged vial. The purity of this fraction was checked by HPLC with the HPLC system used for purification of [^{14}C]crotonaldehyde. Column effluent was collected in fractions and the ^{14}C in each fraction was measured by liquid scintillation spectrometry. If further purification was necessary

the process was repeated. The radiochemical purity of the purified [^{14}C]crotonaldehyde used for all studies was $\geq$96% (Figure 3).

2.4 Dosing

Oral doses were administered by gavage into the stomach. Animals were dosed at the following dose levels: 35, 3.1 and 0.67 mg of [^{14}C]crotonaldehyde per kg body weight. Rats were fasted overnight prior to oral dosing.

Intravenous doses were administered in one of the lateral tail veins. Each dose consisted of ca. 1 mL of 10% ethanol in water (with the exception of 4 animals which were administered the dose in 2% aqueous ethanol containing 2.6 - 2.9 mg [^{14}C]crotonaldehyde/kg body weight. Except for 8 animals (rats 151-1 to 151-4 and 152-1 to 152-4), rats were dosed in closed metabolism chambers in order to trap rapidly expired $^{14}CO_2$. Doses were injected into veins in the tails, which were exteriorized through small openings in the sides of the chambers. After the dose was administered the rats were allowed to draw their tails into the chambers and the opening quickly sealed.

Oral Doses. The specific activity of the [^{14}C]crotonaldehyde was adjusted by combining appropriate amounts of unlabeled crotonaldehyde with purified [^{14}C]crotonaldehyde (in the HPLC mobile phase consisting of 10% EtOH in H_2O) so that the correct amount of crotonaldehyde for dosing was contained in ca. 1 mL of the dose formulation. Oral doses were prepared in argon-purged vials sealed with teflon-faced silicone septum caps and wrapped with aluminum foil. Dosing solutions were administered within 2 h of their preparation. Each dose was drawn into a 1mL Plastipak disposable syringe fitted with a dry gavage needle. The filled syringe was then weighed. After dosing, the needle was

wiped free of mucus and the empty syringe and needle reweighed. Each dose was calculated as the difference between the weights of the filled and empty dosing apparatus. An aliquot of the dose formulation was removed after each 1 mL dose was administered in order to determine the amount of [^{14}C]crotonaldehyde in each dose. This was necessary because of the volatility of crotonaldehyde. The purity of the dosing solution was assayed by HPLC after all the animals had been dosed.

Intravenous Doses. Intravenous dose formulations were prepared as described for the oral dose formulations. One group of rats however, rats 4188-152-1 thru 4, was administered the dose in 2% ethanol in water rather than 10% ethanol. This dose formulation was prepared by diluting the mobile phase containing the purified [^{14}C]crotonaldehyde with 4 volumes of distilled water. Unlabeled crotonaldehyde was then added to give a dosing formulation containing ca. 1.1 mg crotonaldehyde/mL.

2.5 Collection of Biological Samples

Urine and feces were collected separately over the time intervals listed in Tables 5 and 6. Urine was collected in round-bottom flasks over dry ice. Feces were collected in tail cups secured to the rats with surgical adhesive. Urine and feces were stored in the dark at -20°C until analyzed.

Breath was collected by two different trapping methods. In Method A, which trapped volatile organics and CO_2, air was pulled through the metabolism cages at 200-500 mL/min and then through a series of 3 traps. The first contained ca. 75 mL of 95% ethanol in water maintained in ice water. The second contained ca. 75 mL of 1% crotonaldehyde in 2-propanol (v/v) maintained in a dry ice-acetone bath. The third trap contained 400 mL of 1N sodium hydroxide maintained at ambient temperature.

In Method B, which trapped $^{14}CO_2$ only, air was pulled through the metabolism cage at 200-500 mL/min and then through a series of two traps, each containing 400 mL of 1N sodium hydroxide maintained at ambient temperature. The traps were changed over the time intervals listed in Tables 5 and 6. Breath trap solutions were stored at room temperature until analyzed.

At the end of each experiment, the animal was anesthetized with an i.p. injection of 60 mg/kg ketamine and 8.6 mg/kg xylazine. Blood was then withdrawn by cardiac puncture until death occurred. Tissue samples were collected and stored in the dark at -20°C until analyzed.

2.6 Analysis of Samples

2.6.1 Analysis of Biological Samples for Total Radioactivity

Duplicate aliquots of urine and trapping solution from the breath traps were added to 10 mL of scintillation cocktail [toluene:Triton X 100 (2:1) containing 6 g of Omnifluor (New England Nuclear) per liter]. Water or methanol was added as needed to obtain homogenous samples. Feces and livers were homogenized with a Brinkmann Polytron homogenizer. Aliquots of the homogenized feces and livers as well as blood, entire small tissues, and portions of muscle, skin and adipose tissues were burned in a Packard Model 306 sample oxidizer. The resulting CO_2 was trapped in Carbo-Sorb to which Permafluor V scintillation cocktail (both from Packard Instruments) was added. Where possible, analyses for each animal were performed in duplicate.

Samples containing Carbo-Sorb or sodium hydroxide were stored overnight in the dark. All samples were then analyzed for ^{14}C in a Packard Model 460C or 3255 scintillation spectrophotometer. Correction for differing amount of quench was performed by the external standard method.

The scintillation spectrometers were checked at least monthly for counting efficiencies and changes in the standard curves for quench correction. The sample oxidizer was checked for efficiency of recovery daily. It was maintained so that efficiencies for standards were >97%.

2.6.2 Analysis for Samples for [^{14}C]Crotonaldehyde

Filtered aliquots of urine and plasma were analyzed directly by HPLC using a Du Pont Zorbax ODS (0.46 x 25 cm) column and a mobile phase of 5:95 EtOH:0.05 M NH_4OAc (v:v), pH 3.5. The mobile phase flow rate was 1 mL/min. Column effluent was collected in fractions and the ^{14}C eluting in each fraction was measured by scintillation spectrometry.

Skin, adipose, muscle and liver were extracted at 0°C with 50% ethanol in water. The tissue-ethanol mixtures were homogenized with a Brinkmann Polytron homogenizer and then centrifuged at 1600 x g for 5 min. The supernatants were filtered through a 0.2 μm membrane before injection onto the HPLC. A Du Pont Zorbax ODS column was used with a mobile phase consisting of mixtures of ethanol and water. The concentration of ethanol remained constant at 30% for 7.5 minutes following injection and then changed from 30% to 90% over a 1.5 minute gradient. The mobile phase flow rate was 1 mL/min. Column effluent was collected in fractions and analyzed by scintillation spectrometry.

Residues from tissue extraction were oxidized in a Packard 306 oxidizer for total ^{14}C by the same method described in Section 2.6.1.

2.6.3 Analysis of Urine Sample by HPLC/Mass Spectrometry

The 2 - 6 h urine sample from rat 4275-130-4 (cf Table A8) was selected for analysis.. This rat had been given a 2.8 mg/kg intravenous dose of [^{14}C]crotonaldehyde. The 2 - 6 h urine sample contained 42% of the administered ^{14}C.

An 8.0 mL aliquot of urine was lyophilized. Methanol was added to the residue and, after vigorous mixing, the suspension was centrifuged. The methanolic extract was concentrated to ca. 100 µL and recentrifuged. Aliquots of the methanolic solution were then analyzed by radio-HPLC and by HPLC/mass spectrometry. The chromatographic system was identical to that described in section 2.6.2 except that methanol was used in the mobile phase in place of ethanol.

2.7 Stability of [^{14}C]Crotonaldehyde in Stomach Contents

A male F344 rat was sacrificed by decapitation and its stomach excised. Stomach contents were removed and a 20% (w/w) homogenate was prepared by adding the appropriate amount of normal saline and homogenizing the resultant mixture. The homogenate was placed in a 37°C shaker bath and allowed to equilibrate for 5 min, then spiked with a 0.809 mg/g solution of [^{14}C]crotonaldehyde in 10% ethanol in water.

The amount of crotonaldehyde in the spike was equivalent to a 1.8 mg/kg body weight dose. At 5, 30, 60 and 120 min, 1.0 mL aliquots of the homogenate were removed. Aliquots were centrifuged at 1600 x g for 5 min. The supernatant was then passed through a 0.2 µm filter. Particulate matter remaining was oxidized in a Packard 306 oxidizer as described in Section 2.6.1. Aliquots of the filtrate were assayed for total ^{14}C by scintillation spectroscopy. Additional aliquots were assayed for [^{14}C]crotonaldehyde by HPLC. Radioactivity in the column effluent was monitored with a Berthold Model LB503 radioactivity detector. In addition, fractions of column effluent were collected from the 2 h sample and assayed for ^{14}C by scintillation spectrometry.

2.8 In Vitro Metabolism of [^{14}C]Crotonaldehyde in Plasma

Blood was obtained from male F344 rats by cardiac puncture and centrifuged at 1600 x g for 20 min to obtain plasma. One mL of plasma was pipetted into a silanized 1/2 dram vial and sealed with a teflon-faced septum cap. The vial was placed in a 37°C shaker bath and allowed to equilibrate for 5 min. Then a 100 µL aliquot of purified crotonaldehyde in 10% ethanol in water was delivered to the vial to give an incubation mixture containing 7.33 µg crotonaldehyde/g of mixture. Aliquots of plasma were taken at 5 minutes, 0.5, 1, 2, 4, and 20 h and injected directly onto the HPLC column. Column effluent was collected in fractions and assayed for ^{14}C by scintillation spectrometry. The percentage of [^{14}C]crotonaldehyde remaining in the plasma aliquot was calculated by multiplying the percentage of [^{14}C]crotonaldehyde which eluted from the HPLC by the total percentage of ^{14}C which was recovered from the chromatography.

2.9 Records

Until the remaining studies in this contract are completed, the records for this study will be kept in the office or laboratory office of the Study Director. After this time, the records will be stored in the Research Triangle Institute Chemistry and Life Sciences Archives. These records will be stored under the project number for this study (311U-2227). The records will be kept for a minimum of 10 years following the completion of the study.

3.0 Results and Discussion

3.1 In Vitro Experiments

Crotonaldehyde was only slightly degraded by stomach contents. After a 5 min incubation of homogenized stomach contents (20% w/v in normal saline) containing [^{14}C]crotonaldehyde in an amount corresponding to a dose of 1.8 mg/kg, 96% remained as unreacted crotonaldehyde. After 2 h, 94% remained as crotonaldehyde, 1% of the ^{14}C was converted to a more polar compound and 5% of the ^{14}C was bound to the particulate matter (Table 2). Therefore, it is likely that the material being absorbed from the gut was almost entirely crotonaldehyde.

Although crotonaldehyde was fairly stable to stomach contents, it was not stable to plasma enzymes. After only a 5 min incubation of crotonaldehyde with rat plasma at 37°C, less than half of the initial ^{14}C was accounted for by the parent compound (Table 3, Figure 4). By the end of 30 min, the amount of parent crotonaldehyde had decreased to 15% of the initial value. The percentage of parent compound remaining in the incubator mixture then slowly decreased to 8% of the initial value as the incubation time was increased to 20 h. This rapid initial reaction of crotonaldehyde followed by a much slower rate of reaction is consistent with either the depletion of the substrate(s) with which crotonaldehyde is reacting or the deactivation of the enzyme(s) mediating the reaction. If either process is occurring, then reaction of crotonaldehyde in a dynamic *in vivo* situation would be expected to be even more rapid and to go to completion (i.e., no unreacted crotonaldehyde remaining).

3.2 In Vivo Studies

3.2.1 Dose Selection

Oral doses were administered at rates of 35, 3.3 and 0.67 mg/kg. The highest dose was approximately 0.1 times the LD_{50} (Smyth and Carpenter, 1944). Intravenous doses were administered at 2.8 mg/kg. This dose produced mild, but observable, short term discomfort in some of the animals. Higher intravenous dose levels were thus not attempted.

Purified [^{14}C]crotonaldehyde was available as a solution in 1:9 ethanol:water. Due to the low concentration of [^{14}C]crotonaldehyde in this solution, its volatility and its instability, we were not able to separate the crotonaldehyde from the solvent. The solvent mixture was thus used as part of the dose vehicle. In order to determine whether the ethanol in this solvent mixture had an effect on the metabolism of crotonaldehyde (for example, by overloading the alcohol/aldehyde dehydrogenase enzymes), a study was conducted which compared the metabolism of crotonaldehyde injected intravenously in 10% ethanol with that injected in 2% ethanol. The results of this study (cf Tables 7 and 8) show that there is no difference in the metabolism of crotonaldehyde due to the increased amount of ethanol.

3.2.2 Excretion of Crotonaldehyde and Its Metabolites

The average cumulative excretions of total ^{14}C in urine, feces, and breath following administration of [^{14}C]crotonaldehyde are shown in Tables 4-7. Breath and urine were the major routes of excretion of ^{14}C following oral or intravenous administration. After a 2.8 mg/kg intravenous dose, an average of 48% of the dose was excreted in urine, 41% in breath as CO_2, and 0.3% in feces in 72 h (N=3). An average of 37% of a 2.6-2.9 mg/kg IV dose was excreted in urine and 31% in breath as CO_2 in 6 h (N=13).

In oral studies at doses of 0.67, 3.3 and 35 mg/kg of [^{14}C]crotonaldehyde, 38-39% of the dose was excreted in urine, 44-49% in breath as CO_2 and 6-7% in feces in 72 h. There was no change in excretion pattern over this dose range. The amount of ^{14}C excreted in feces is equivalent to the amount not absorbed into the systemic circulation since virtually no ^{14}C was excreted in feces after intravenous doses of [^{14}C]crotonaldehyde. Thus the amount of [^{14}C]crotonaldehyde that was absorbed from oral doses was $\geq$93% in all studies. The percent dose excreted in feces (6-7%) was consistent with the small percentage of the ^{14}C in the *in vitro* study that was bound to the stomach contents.

HPLC analysis of the combined 0-72 h urine samples showed that essentially no unmetabolized crotonaldehyde was excreted in urine. This result is consistent with the rapid reaction of crotonaldehyde observed *in vitro* in plasma. The rapid excretion of the metabolites in urine (and as CO_2 in breath) makes it unlikely that a significant amount of crotonaldehyde was covalently bonded to macromolecules.

Typical HPLC radiochromatograms of the combined urines are shown in Figures 5 (intravenous dose) and 6 (oral dose). Two incompletely resolved peaks of radioactivity which account for 65-80% of the total ^{14}C are present in each chromatogram. The materials in these peaks are less retained on the reverse phase column than either crotonaldehyde or crotonic acid (and are therefore probably more polar than these standards). Lesser amounts of several even more polar metabolites are also present. The excretion of ^{14}C in the form of quite polar metabolites of crotonaldehyde supports the findings of Gray and Barnsley (1971), who identified 3-hydroxy-1-methylpropylmercapturic acid (Compound 1, Figure 7) and 2-carboxy-1-methylethylmercapturic acid (Compound 2, Figure 7) as urinary metabolites of crotonaldehyde in rats.

Combined HPLC/mass spectral analysis (thermospray inlet system) was performed on a sample of rat urine in order to better define the nature of the major urinary metabolites. The urine sample selected for this analysis (rat 4275-130-4; cf Table A8) contained 42% of the dose of ^{14}C and had a metabolite profile (Figure 8) similar to those observed for the 0-72 h combined urines for the other animals. Mass spectra of the column effluent obtained at times corresponding to the retention times of the two major urinary metabolites are shown in Figures 9 and 10, respectively. Both spectra contain prominant signals at m/z 236, which corresponds to the molecular ion $+H^+$ of 3-hydroxy-1-methylpropylmercapturic acid and at m/z 253, which corresponds to the molecular ion $+NH_4^+$ of the same compound. Signals arising from molecular ions $+H^+$ and $+NH_4^+$ would be expected since the HPLC mobile phase contained NH_4OAc as a buffer. Signals at m/z 133 and 150 are also seen in these spectra, which could be attributed to the fragment ion $\underline{3}$ and $\underline{3} + NH_3$ (Figure 7; Milne et al, 1970). Single ion plots of m/z 236 and 253 (Figure 11) show that the intensities of these ions rise and fall at times corresponding to those for the elution of the major crotonaldehyde metabolites. Single ion plots of the m/z 133 and 150 ions (Figure 11) show that the intensities of these ions are correlated somewhat with the elution times of the major metabolites but with profiles that are not as closely matched to the metabolite elution times as those of the ions at m/z 236 and 253.

The presence of two metabolite peaks with protonated molecular ions at m/z 236 could be due to one of at least 3 different possibilities: (1) Reaction of crotonaldehyde with glutathione occurs in a nonstereospecific manner, giving rise to diastereomers. These diastereomers

would then be degraded to a pair of diasteromers of 1, which could be separated by HPLC. (2) Reaction of crotonaldehyde with glutathione could result in attachment of the sulfur to C_1 of the crotonaldehyde in addition to C_3 as in the metabolites shown in Figure 7 to form a positional isomer of 1. (3) This ion at m/z 236 is not the protonated molecular ion of (at least) one of the metabolites, but is a fragment ion of the molecular ion (the latter not being observed). While the formation of separable diastereomers seems to be the most likely of these possibilities, additional work would be required to conclusively identify the major urinary metabolites of crotonaldehyde from our study.

Excretion of ^{14}C in breath was essentially entirely as $^{14}CO_2$. The very small amounts (<1.5% of dose) of ^{14}C trapped in the cryogenic (organic vapors) trap may also be $^{14}CO_2$ dissolved in the 2-propanol trapping solution.

3.2.3 Distribution of [^{14}C]Crotonaldehyde and Its Metabolites in Tissues

Concentrations of ^{14}C-labeled compounds in tussies after oral and intravenous administration of [^{14}C]crotonaldehyde are shown in Tables 9-14. Over the time period examined following intravenous dosing (0.25 - 72 h) the concentration of ^{14}C in skin, muscle, adipose and liver never exceeded that in blood. As would be expected for a relatively polar, water soluble compound, concentrations of ^{14}C in adipose were low, rising to only ca. one-fourth of that in blood at the long time points. Concentrations of ^{14}C in trachea, lungs and adrenals exceeded that in blood for at least two time points, but these concentrations never rose to more than 1.6 times that in blood. Elimination of ^{14}C from blood and tissues was rapid initially, with half-lives of ca. 1 h or less. This

was followed by much slower elimination of the last ca. 10% of the dose, which occurred with half-lives of 2.5 days or longer.

The percent of oral doses in tissues 72 h after dosing was essentially the same for doses of 35 and 0.67 mg/kg, except for the stomach (which contained 0.2% and 0.8% of these doses, respectively). Tissue-blood ratios (TBR) were somewhat higher in these studies than they were after intravenous administration of the [^{14}C]crotonaldehyde. Tissues with TBR values between 1.0 and 2.0 included skin, intestines, seminal vesicles, prostate, lungs, spleen, kidney and heart. Higher TBR values were observed in the adrenals (3.4 and 4.6), trachea (2.0 and 2.3), stomach (3.9 and 14), esophagus (3.0 and 4.4), and liver (2.9 and 7.1).

The amount of unmetabolized crotonaldehyde was determined in plasma, skin, muscle, adipose and liver 0.25 h after intravenous dosing. A typical HPLC radiochromatogram of plasma is shown in Figure 12. In all cases, essentially no crotonaldehyde was found ($\leq$1% of the ^{14}C present in the tissue eluted from the HPLC column with the same retention time as crotonaldehyde).

4.0 References

E. Boyland and L. F. Chasseand, Biochem. J., 104 95 (1970).

J. M. Gray and E. A. Barnsley, Xenobiotica 1, 55 (1971).

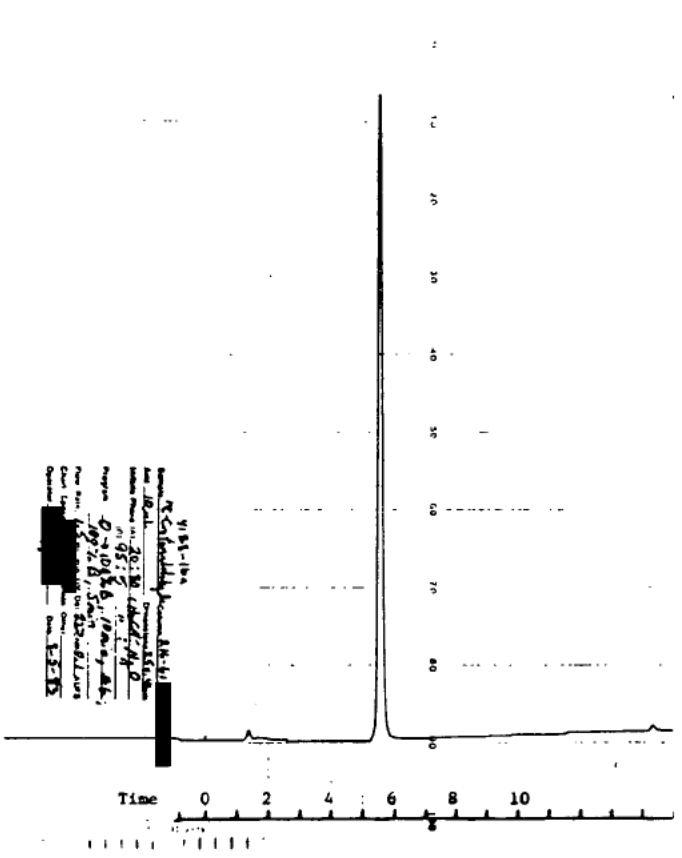
G. W. A. Milne, T. Axenrod and H. M. Fales, J. Am. Chem. Soc., 92, 5170 (1970).

Figure 1. HPLC Purity Check of [^{14}C]Crotonaldehyde (MRI Lot No. 83-127-16-30)

Chromatographic Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- (A) 20:80 Acetonitrile:Water (v/v) (B) 95:5 Acetonitrile:Water (v/v)
Solvent Program	- 0%B to 100%B in 10 min over a linear gradient
Flow Rate	- 1.5 mL/min
Fraction Interval	- 1 minute

R_t of Crotonaldehyde = 5.4 min (fraction 6)



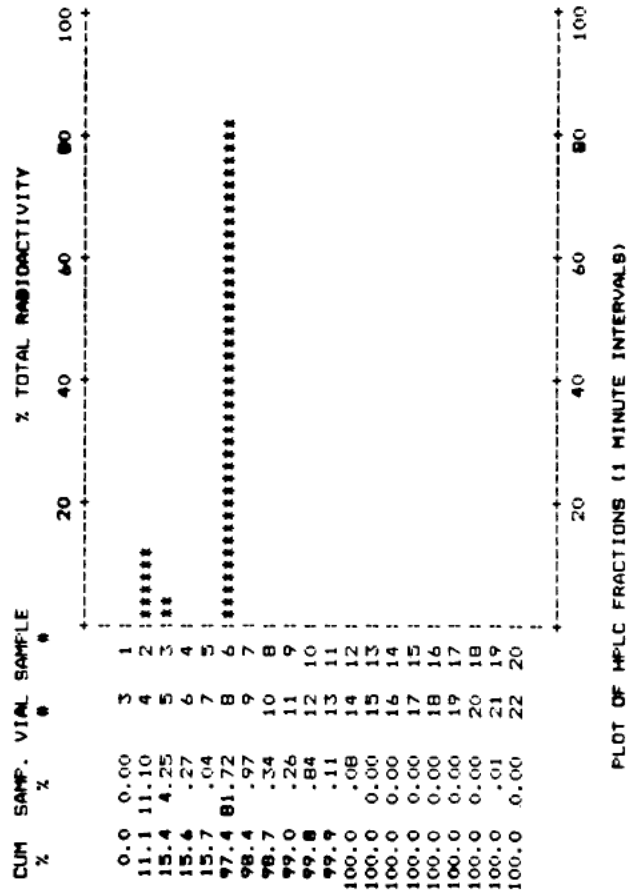


Figure 2. HPLC of Unlabeled Crotonaldehyde
(Aldrich, Lot No. 1217PH)

Chromatographic Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- (A) 20:80 Acetonitrile:Water (v/v) (B) 95:5 Acetonitrile:Water (v/v)
Solvent Program	- 0%B to 100%B in 10 min over a linear gradient
Flow Rate	- 1.5 mL/min
R_t of Crotonaldehyde	= 5.4 min

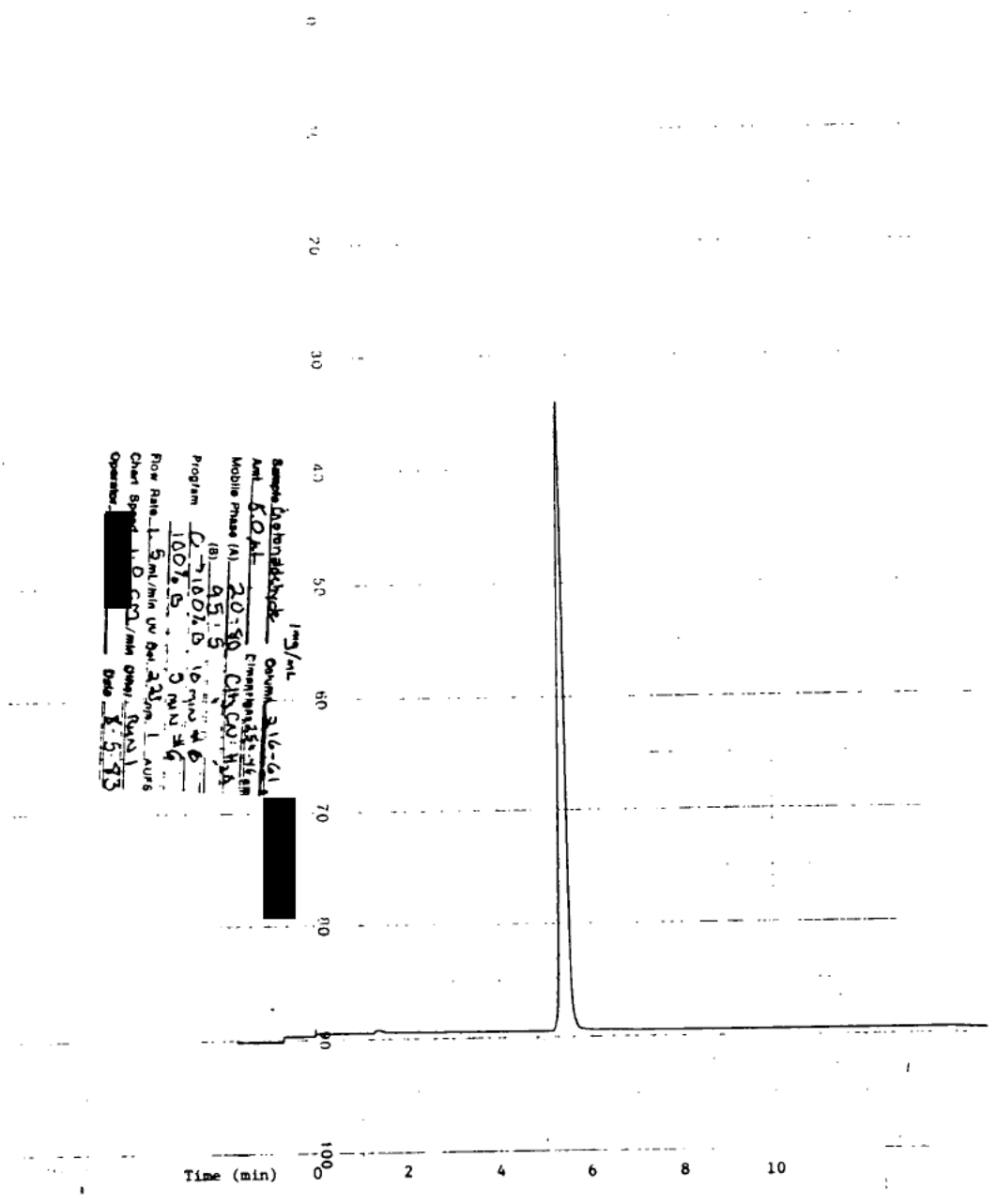
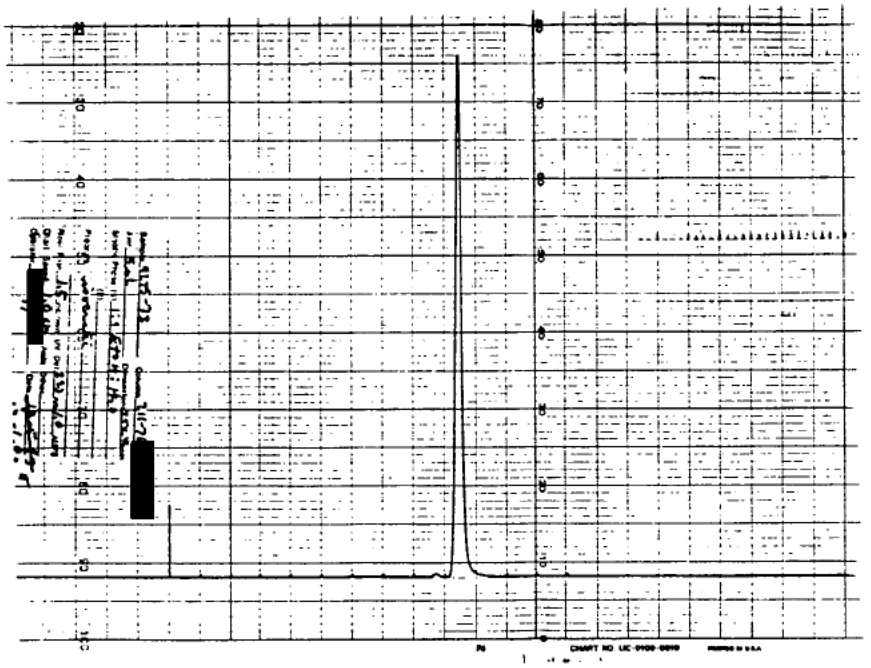


Figure 3. Representative HPLC Purity Check of Purified [^{14}C]Crotonaldehyde

HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- 10:90 Ethanol:Water (v/v)
Solvent Program	- Isocratic
Flow Rate	- 1.5 mL/min
Fraction Interval	- 1 min

R_t of Crotonaldehyde = 9.5 min (fraction 10)



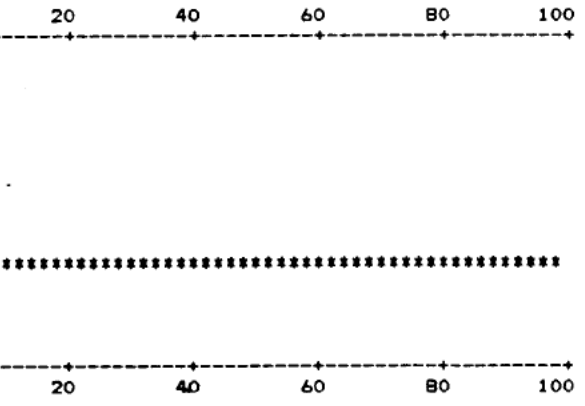
PURITY OF 4275-73

FIRST VIAL # = 24 LAST VIAL # = 36

DPM SUMMATION = 52381.9

CUM %	FRAC. %	VIAL #	FRACTION #
.0	.00	24	1
.1	.05	25	2
.3	.25	26	3
.5	.22	27	4
.5	0.00	28	5
.5	0.00	29	6
.5	0.00	30	7
.5	0.00	31	8
1.3	.77	32	9
99.2	97.94	33	10
99.8	.57	34	11
100.0	.16	35	12
100.0	.03	36	13

% TOTAL RADIOACTIVITY



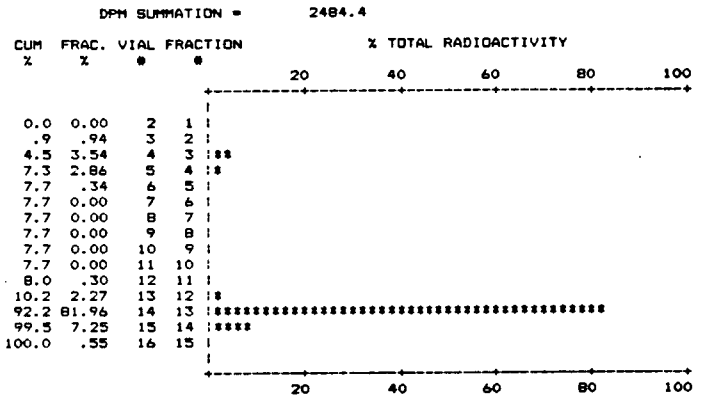
PLOT

Figure 4. Radiochromatograms of Plasma after In Vitro Metabolism of [^{14}C]Crotonaldehyde

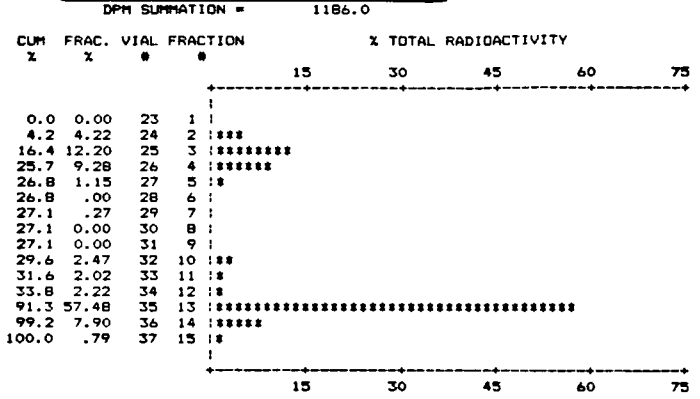
HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax
Mobile Phase	- 5:95 EtOH:0.05 M NH_4OAc at pH 3.5
Solvent Program	- Isocratic
Flow Rate	- 1.5 mL/min
Fraction Interval	- 1 min
R_t of Crotonaldehyde	= 12.8 min (fractions 13 & 14)

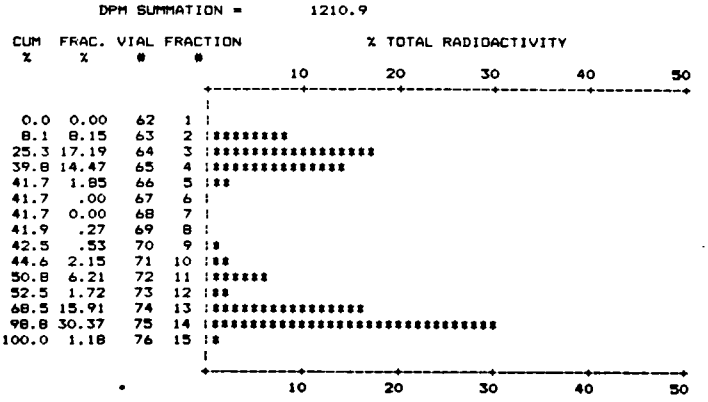
A. 5 minute incubation



B. 30 minute incubation



C. 2 hour incubation



D. 20 hour incubation

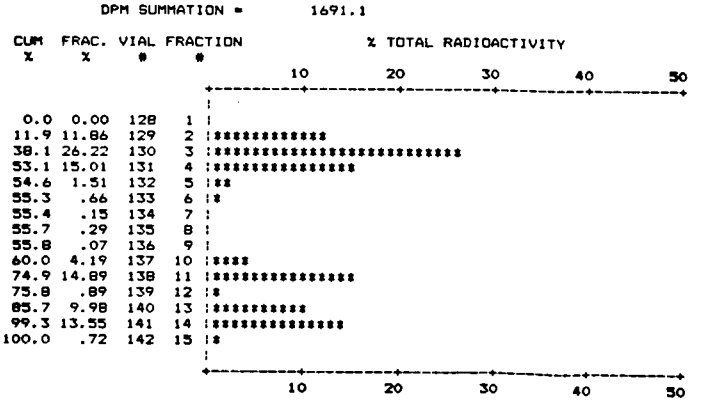


Figure 5. Typical HPLC Radiochromatogram of 0-72 h Urine Composite Following a 2.8 mg/kg Intravenous Dose of [^{14}C]Crotonaldehyde

HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- 5:95 EtOH:0.05 M NH_4OAc at pH 3.5
Solvent Program	- Isocratic
Flow Rate	- 1 mL/min
Fraction Interval	- 1 min (fractions 9-28 collected over 0.2 min intervals)
R_t of Crotonaldehyde	= 18.4 min (fractions 34 & 35)
Recovery of ^{14}C	- 99%

DPM SUMMATION = 5509.5

CUM %	FRAC. %	VIAL #	FRACTION #	% TOTAL RADIOACTIVITY (5 10 15 20 25)
.2	.16	93	1	
.2	0.00	94	2	
5.4	5.29	95	3	**********
9.5	4.06	96	4	********
10.3	.75	97	5	**
10.7	.43	98	6	*
10.8	.13	99	7	
10.9	.04	100	8	
11.1	.26	101	9	*
12.7	1.62	102	10	***
15.2	2.49	103	11	*****
16.4	1.17	104	12	**
16.8	.42	105	13	*
17.3	.47	106	14	*
23.7	6.38	107	15	**********
38.3	14.59	108	16	**********
48.7	10.39	109	17	**********
63.9	15.23	110	18	**********
83.4	19.52	111	19	**********
92.5	9.03	112	20	**********
95.9	3.45	113	21	*******
97.1	1.22	114	22	**
97.8	.72	115	23	*
98.3	.50	116	24	*
98.6	.21	117	25	
98.7	.13	118	26	
98.8	.11	119	27	
98.9	.07	120	28	
99.3	.43	121	29	*
99.6	.35	122	30	*
99.9	.26	123	31	*
100.0	.05	124	32	
100.0	0.00	125	33	
100.0	0.00	126	34	
100.0	0.00	127	35	
100.0	.04	128	36	

(5 10 15 20 25)

Figure 6. Typical HPLC Radiochromatogram of 0-72 h Urine Composite Following 33 mg/kg Oral Dose of [^{14}C]Crotonaldehyde

HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- 5:95 EtOH:0.05 M NH_4OAc at pH 3.5
Solvent Program	- Isocratic
Flow Rate	- 1 mL/min
Fraction Interval	- 1 min (fractions 9-28 collected over 0.2 min intervals)
R_t of Crotonaldehyde	= 18.6 min (fractions 34 & 35)
Recovery of ^{14}C	- 99%

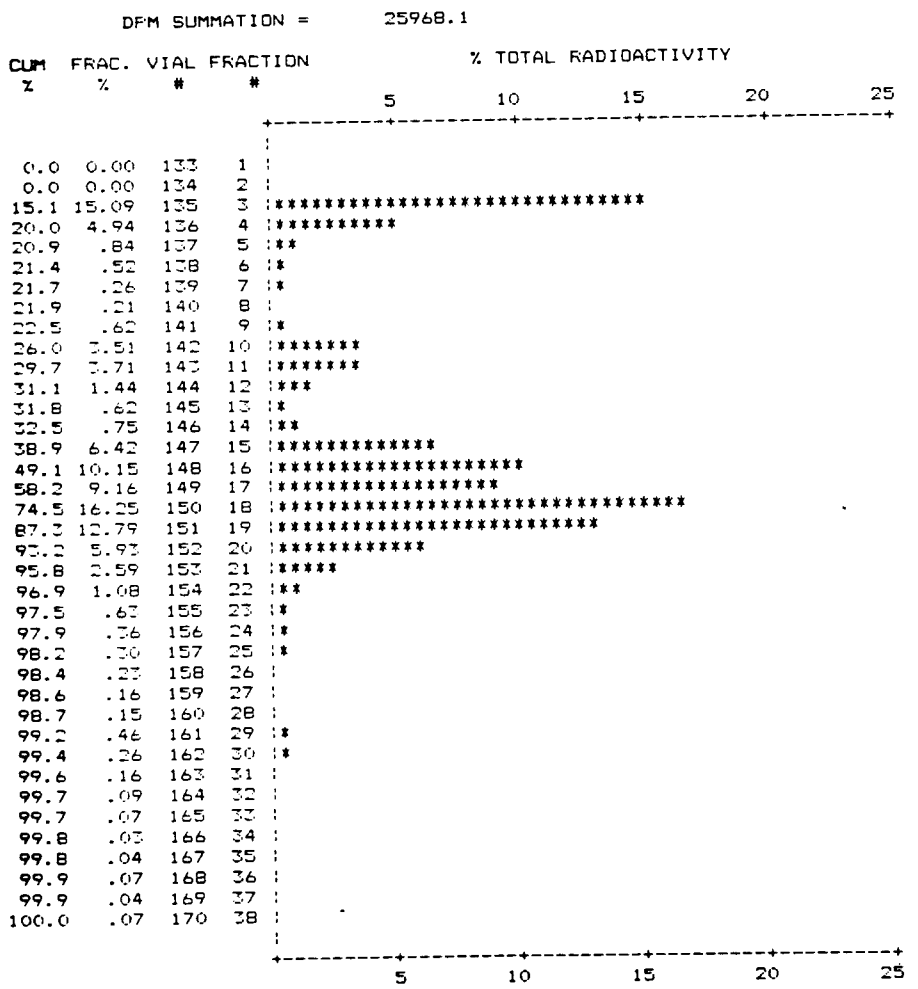
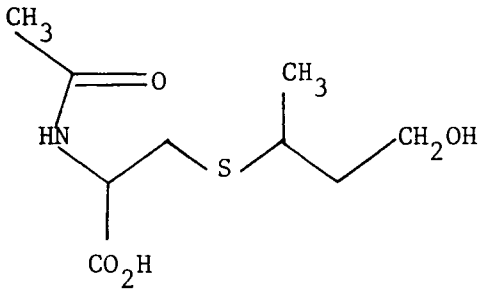
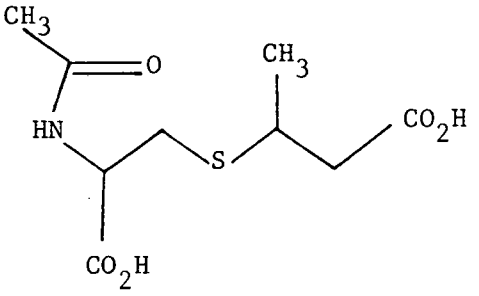


Figure 7. Structures of Urinary Metabolites of Crotonaldehyde and a Possible Mass Spectral Fragment



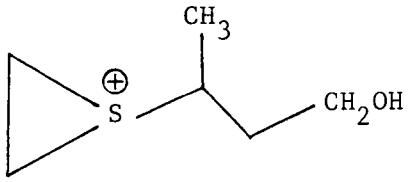
3-hydroxy-1-methypropylmercapturic acid (MW = 235)

1



2-carboxy-1-methylethylmercapturic acid (MW = 249)

2



3

Figure 8. HPLC-Radiochromatogram of Urine Sample Used for Combined HPLC/MS Examination

HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- 5:95 Methanol:0.05 M NH_4OAc at pH 3.5
Solvent Program	- Isocratic
Flow Rate	- 1 mL/min

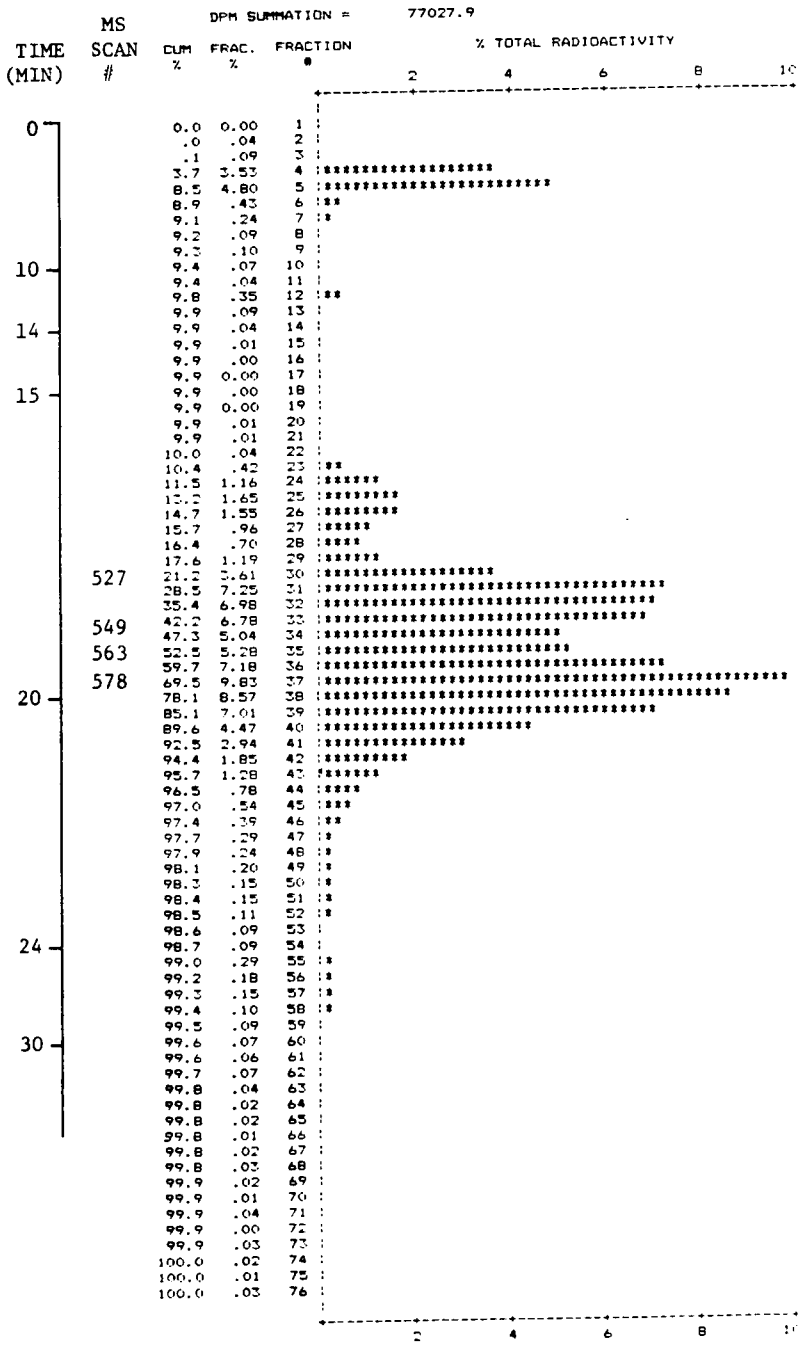


Figure 9. Summation of Mass Spectral Scans 545-562 (Less Background) From the HPLC/Mass Spectra of Rat Urine

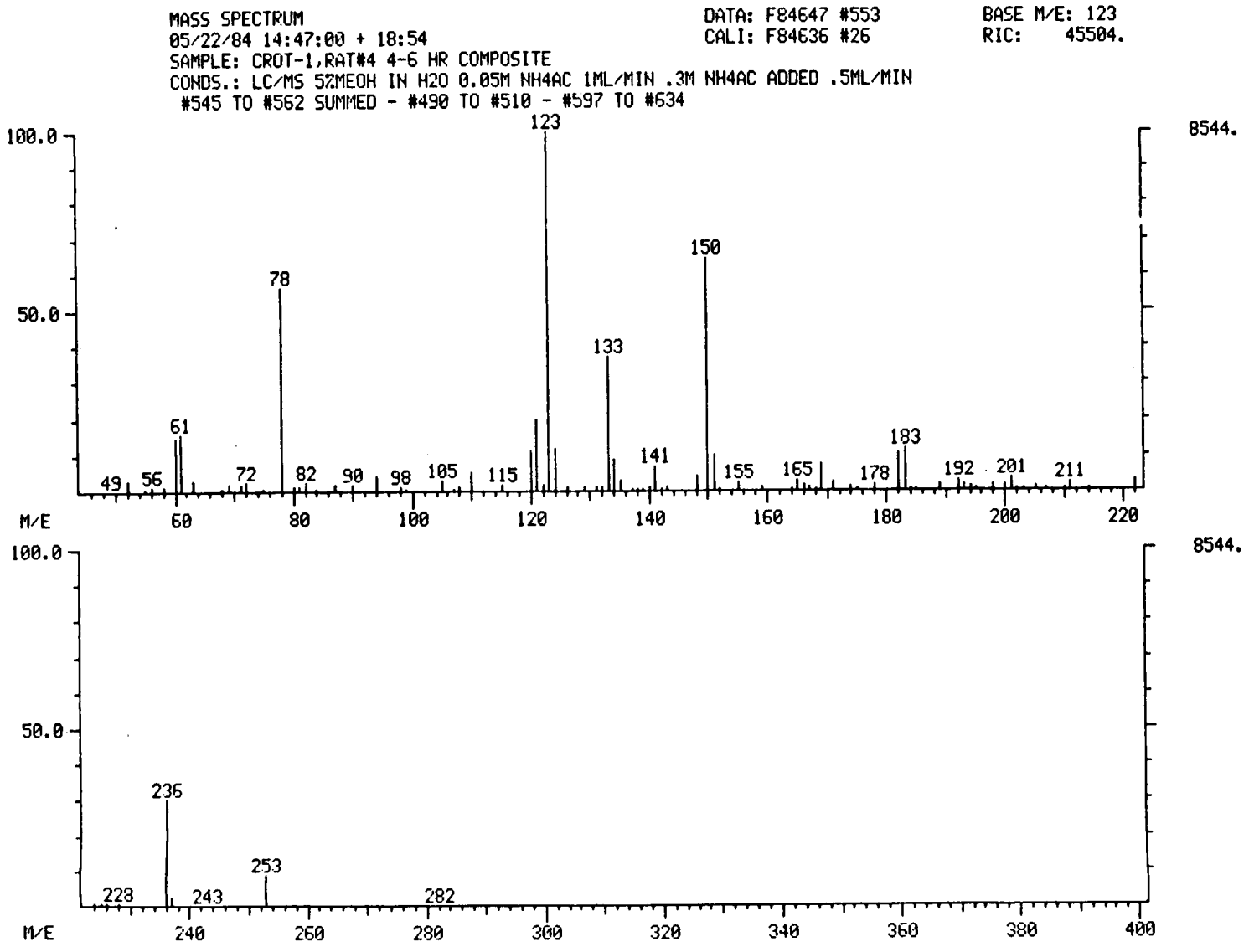


Figure 10. Summation of Mass Spectral Scans 568-573 (Less Background) From the HPLC/Mass Spectra of Rat Urine

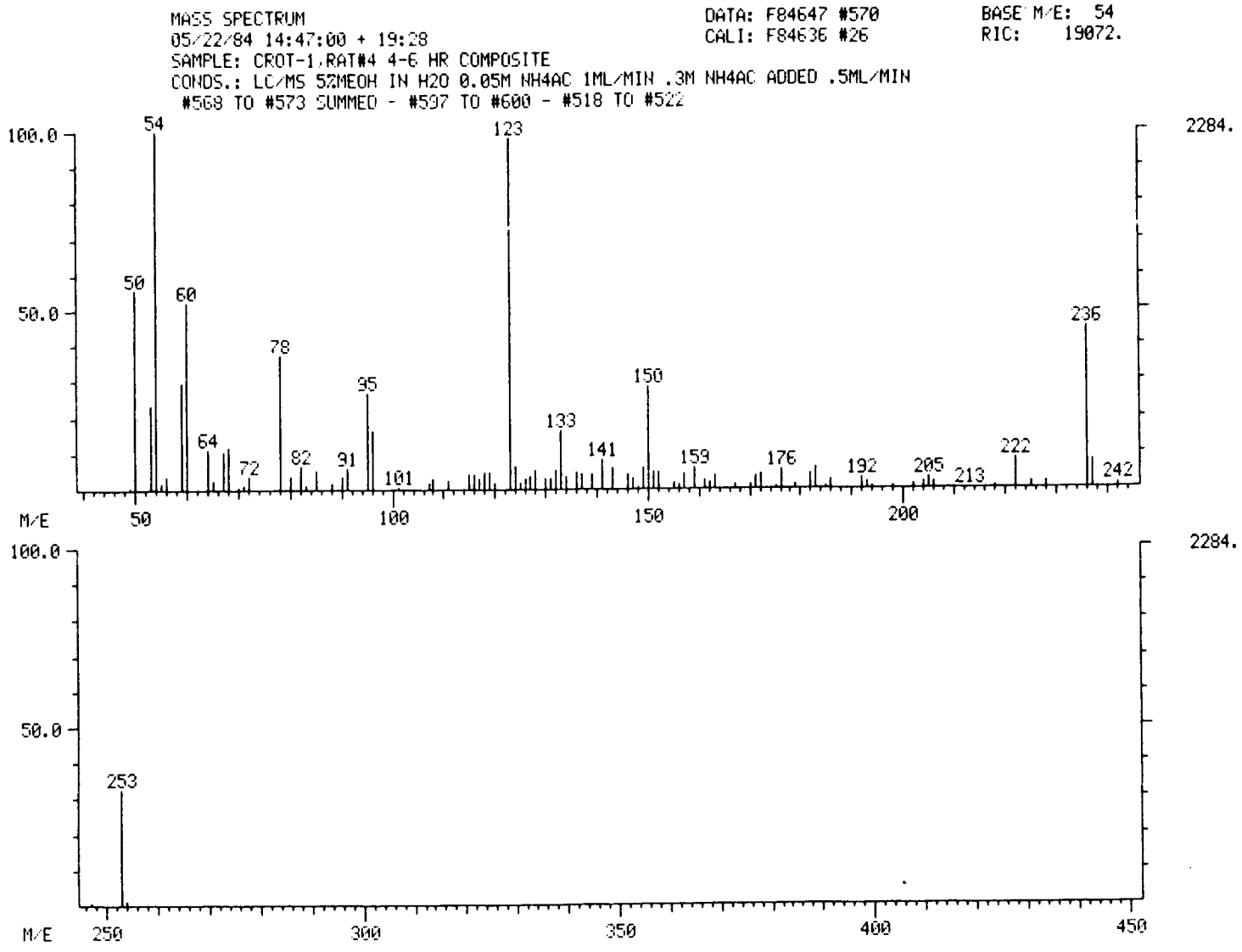


Figure 11. Single Ion Plots From the HPLC/Mass Spectra of Rat Urine.

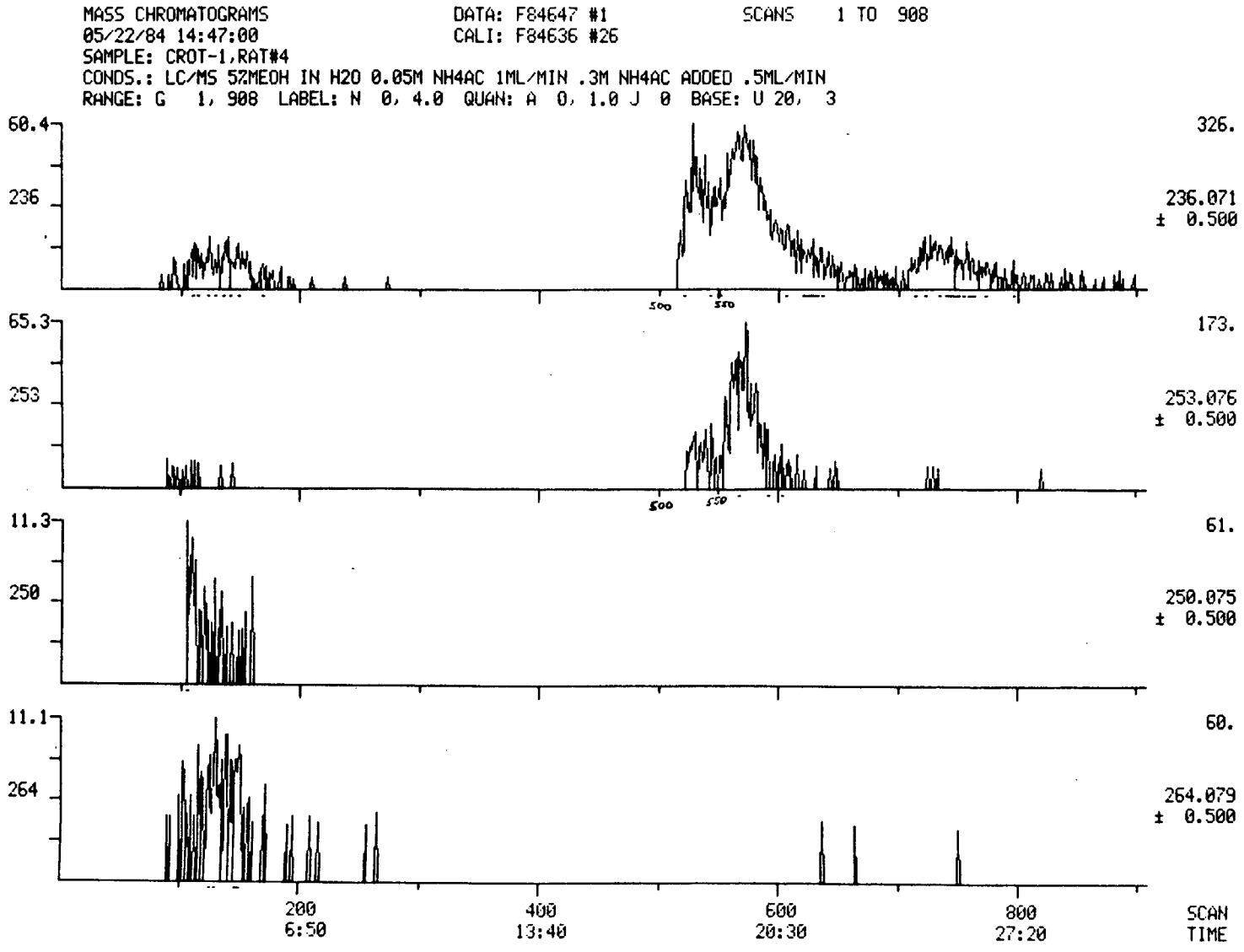


Figure 11 (continued)

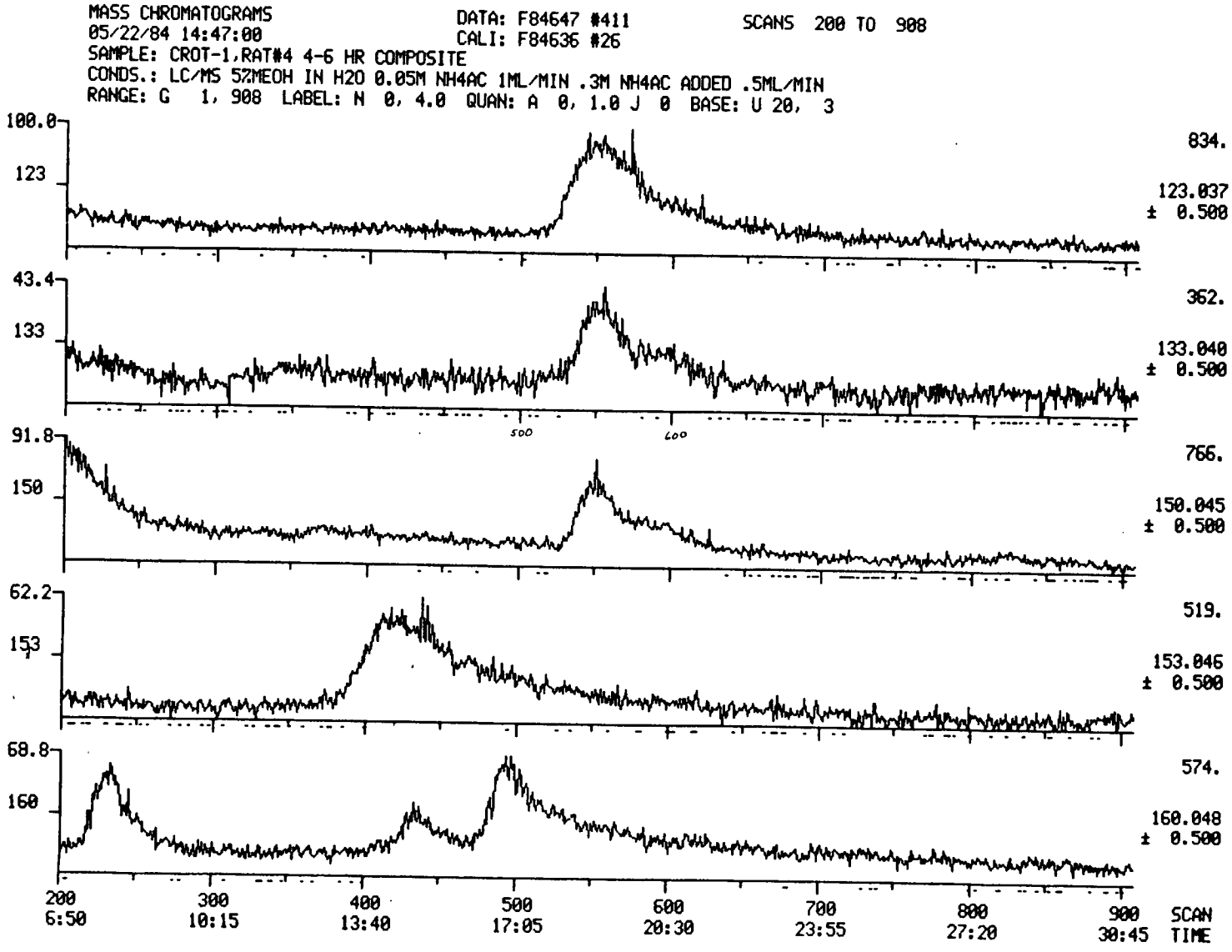


Figure 12. Typical Radiochromatogram of 0.25 h Plasma From a Rat Following a 2.8 mg/kg Intravenous Dose of [^{14}C]Crotonaldehyde

HPLC Conditions:

Column	- 0.46 x 25 cm Dupont Zorbax ODS
Mobile Phase	- 1:9 EtOH:H_2O
Solvent Program	- Isocratic
Flow Rate	- 1.0 mL/min
Fraction Interval	- 1 min

R_t of Crotonaldehyde = 18.6 min (fraction 19)

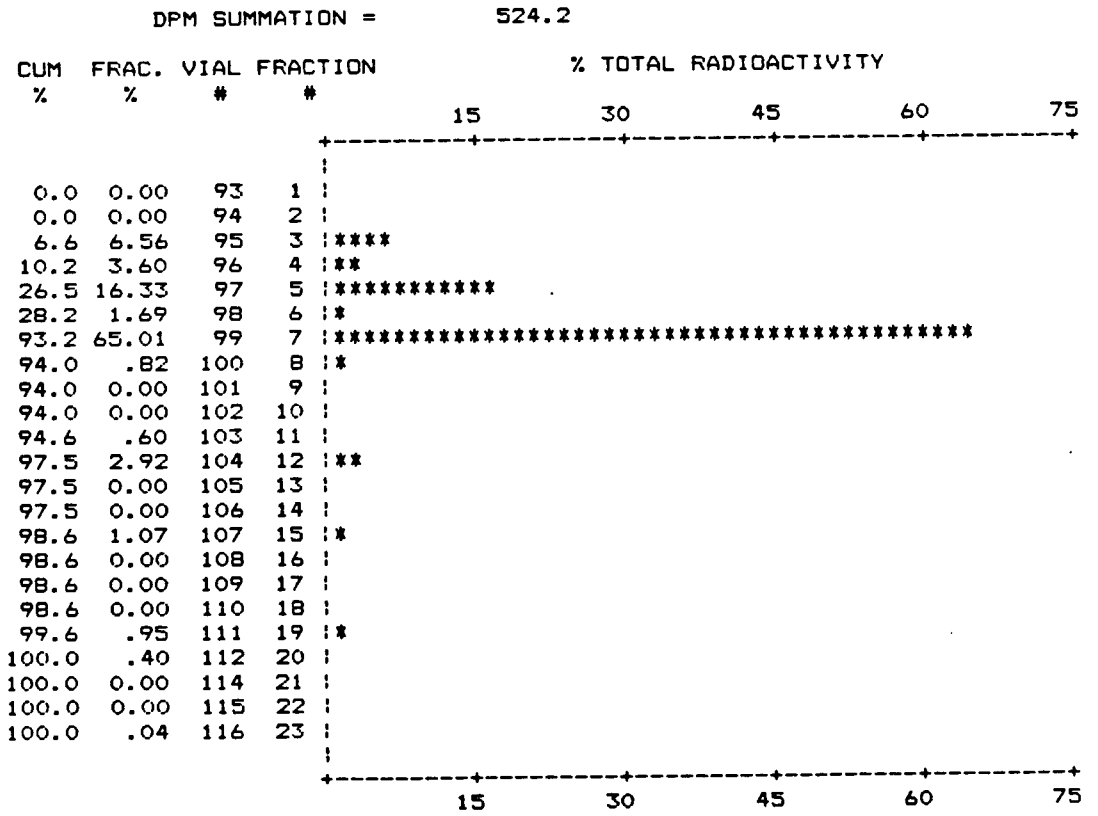


Table 1

Animal Data

Rat No.	Route	Weight of Rat(g)	Dose (mg/kg)	Time of Sacrifice
4188-77-1	Oral	272	39.1	72 h
4188-77-2*[a]		248	33.8	
4188-77-3*		268	36.3	
4188-77-4*		269	32.2	
4188-121-1	Oral	280	3.55	72 h
4188-121-2		286	3.20	
4188-121-3		282	3.13	
4188-121-4		291	3.38	
4188-121-5*	Oral	281	0.715	72 h
4188-121-6*		281	0.663	
4188-121-7*		272	0.638	
4188-121-8		282	0.671	
4275-87-1*	IV	328	2.88	0.25 h
4275-87-2*		325	2.84	
4275-87-3*		330	2.88	
4275-87-4		353	2.72	
4440-152-1	IV[b]	291	2.69	0.25 h
4440-152-2		259	2.92	
4440-152-3		293	2.66	
4275-81-1*	IV	334	2.91	0.75 h
4275-81-2		311	2.84	
4275-81-3*		335	2.74	
4275-81-4*		309	2.89	
4275-57-2*	IV	317	2.91	2 h
4275-57-3*		307	2.99	
4275-57-4*		300	2.88	
4188-178-1*	IV	219	2.62	6 h
4188-178-2*		277	2.57	
4188-178-3*		250	2.60	
4188-178-4		274	2.70	
4188-151-1*	IV	236	2.74	24 h
4188-151-2		229	2.85	
4188-151-3*		232	2.84	
4188-151-4*		233	2.81	

(continued)

Table 1 (continued)

Animal Data

Rat No.	Route	Weight of Rat(g)	Dose (mg/kg)	Time of Sacrifice
4188-152-1	IV[c]	217	3.00	24 h
4188-152-2*		230	2.89	
4188-152-3*		232	2.80	
4188-152-4*		229	2.84	
4275-40-1*	IV	299	2.69	72 h
4275-40-3*		332	2.80	
4275-40-4*		307	2.91	
4275-130-1	IV	239	2.92	72 h
4275-130-2		246	2.76	
4275-130-4		241	2.56	

[a]* indicates that tissues from this animal were examined for total ^{14}C content.

[b]Tissues obtained for extraction.

[c]Dose administered in 2% EtOH.

Table 2. Percentage of [^{14}C]Crotonaldehyde Remaining in Male F344 Rat Stomach Contents/Normal Saline After *In Vitro* Incubation at 37°C

Incubation Time	Percent ^{14}C Remaining in Filtrate (as Crotonaldehyde)	Percent ^{14}C Bound to Particulate Matter
5 min	96	4
30 min	96	4
1 h	95	5
2 h	94	5

Table 3. *In Vitro* Reaction of [^{14}C]Crotonaldehyde with Rat Plasma[a]

Time After Addition of [^{14}C]Crotonaldehyde	Percent of Injected ^{14}C That Eluted From HPLC Column	Percent of [^{14}C]Crotonaldehyde in Column Eluent	Percent of [^{14}C]Crotonaldehyde That Has Not Been Degraded[b]
0 min	97	99	(100)
5 min	45	89	42
30 min	22	66	15
1 h	21	57	12
2 h	22	46	11
4 h	30	32	10
20 h	31	24	8

[a]Initial [^{14}C]Crotonaldehyde concentration was 7.3 μg/mL.

[b]Corrected for recovery of initial [^{14}C]Crotonaldehyde sample.

Table 4

Recovery of Total Radioactivity After Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)[a]

Time (h)	Route	Dose (mg/kg)	Urine	Breath CO_2	Breath Volatiles	Feces	Major Selected Tissues & Blood[b,c]	Total
0.25	IV	2.8	N/A[d]	N/A		N/A	55 ± 1	
0.75	IV	2.8	N/A	N/A		N/A	37 ± 3	
2	IV	2.8	N/A	N/A		N/A	18 ± 0.3	
6	IV	2.6	39 ± 5	35 ± 6	1.3 ± 0.8	N/A	10 ± 0.5	82 ± 4
24	IV	2.8	50 ± 9	34 ± 7		0.55 ± 0.25	7.4 ± 0.4	90 ± 4
24[e]	IV	2.9	45 ± 5	36 ± 1		0.5 ± 0.1	8.7 ± 0.9	88 ± 4
72	IV	2.8	(39 ± 6)[f]	43 ± 4		N/A	4.8 ± 0.5	(88 ± 4)[f]
72	IV	2.8	48 ± 7	41 ± 2		0.27 ± 0.12	N/A	
72	Oral	0.67	39 ± 4[b]	47 ± 5[b]		6.6 ± 0.9[b]	6.2 ± 0.7	99 ± 8[b]
72	Oral	3.3	34 ± 2[b]	49 ± 7[b]		5.6 ± 3.8[b]	N/A	
72	Oral	35	38 ± 3	44 ± 5	0.26 ± 0.19	6.9 ± 0.2	4.7 ± 0.2	93 ± 4

[a] Mean ± SD for four animals except where noted.

[b] Mean ± SD for three animals.

[c] Major tissues are considered to be skin, muscle, adipose, and liver. Skin is assumed to be 15% of total body weight; muscle, 50%; and adipose, 10%.

[d] N/A: Samples were not obtained (or analyzed).

[e] Dose was administered in 2% ethanol.

[f] Due to loss of a portion of some samples, actual value is higher than that shown.

Table 5

Cumulative Excretion of Total ^{14}C After Oral Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	35[a]				3.3[b]				0.67[b]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)												
12	27 ± 10	33 ± 5	d	60 ± 11	32.8 ± 5.6[a]	43.6 ± 5.5[a]	d	76.5 ± 9.6[a]	37.0 ± 4.7	41.0 ± 4.6	d	78.0 ± 7.7
24	35 ± 4	39 ± 4	2.9 ± 2.6	77 ± 7	32.9 ± 2.3	e	5.1 ± 3.7	81.8 ± 5.0	38.7 ± 4.9	44.7 ± 5.2[c]	5.8 ± 1.2	87.4 ± 9.9[c]
36	37 ± 3	42 ± 4		81 ± 4	33.3 ± 2.1	45.4 ± 6.7		83.7 ± 4.9	39.0 ± 4.0	45.0 ± 4.6		89.8 ± 7.1
48	37 ± 3	43 ± 5	5.6 ± 1.1	86 ± 3	33.4 ± 2.1	47.9 ± 6.7[e]	5.5 ± 3.8	86.7 ± 4.8	39.1 ± 4.0	45.7 ± 4.7	6.4 ± 0.9	91.2 ± 7.2
72	38 ± 3	44 ± 5	6.9 ± 0.2	89 ± 3	34.0 ± 1.6	49.1 ± 6.9	5.6 ± 3.8	88.7 ± 4.6	39.4 ± 4.1	46.8 ± 5.0	6.6 ± 0.9	92.8 ± 7.5

[a]Values are mean ± SD for four animals.

[b]Values are mean ± SD for three animals, except where noted otherwise.

[c]Values are mean ± range for two animals.

[d]First feces collection was 0-24 h.

[e]The 12-24 h and the 36-48 h breath samples were accidentally combined before analysis. The percent dose excreted for this combined sample is recorded as one sample, 36-48 h. See data for individual rats in Tables A1 - A3 in Appendix.

Table 6

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	2.8[a]				2.8[b]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)								
0-1	(9.4 ± 7.2)[c]	16.2 ± 2.2	d	25.7 ± 5.4	1.4 ± 1.3	16.6 ± 0.3	e	18.0 ± 1.1
1-2	(13.9 ± 10.5)[c]	26.1 ± 3.2		40.0 ± 7.7	18.0 ± 16.4	26.0 ± 0.5		44.0 ± 16.0
2-4	(22.8 ± 8.0)[c]	32.0 ± 4.0		54.8 ± 9.3		31.1 ± 1.3		
4-6	(28.9 ± 8.7)[c]	34.4 ± 4.4		63.3 ± 8.0	40.2 ± 7.0	33.3 ± 1.4		73.5 ± 6.7
6-12	(36.3 ± 6.0)[c]	37.4 ± 4.4		73.9 ± 5.4	45.4 ± 7.2	36.4 ± 1.8		81.9 ± 6.1
12-24	(38.0 ± 5.7)[c]	39.2 ± 4.8		77.2 ± 5.5	46.8 ± 6.7	38.2 ± 2.2		85.0 ± 5.5
24-36	(38.4 ± 5.7)[c]	40.3 ± 4.7		78.8 ± 5.5	47.2 ± 6.7	39.3 ± 2.3		86.6 ± 5.4
36-48	(38.7 ± 5.7)[c]	41.0 ± 4.9		79.7 ± 5.5	47.4 ± 6.6	40.0 ± 2.3		87.5 ± 5.4
48-72	(39.0 ± 5.6)[c]	42.0 ± 5.0		81.0 ± 5.7	47.7 ± 6.6	40.9 ± 2.5	0.27 ± 0.12	88.8 ± 5.0

(continued)

Table 6 (continued)

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	2.8[a]				2.6[a]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath[f]	Feces	Total
Time (h)								
0-1	0.4 ± 0.8	14.6 ± 3.1	e	15.0 ± 2.9	10.4 ± 10.1	16.4 ± 4.0	d	27.6 ± 11.8
0-2	5.0 ± 10.0	22.4 ± 3.4		27.4 ± 7.3	16.6 ± 11.6	24.5 ± 1.9		42.3 ± 11.5
2-4	21.9 ± 17.6	27.7 ± 5.1		49.5 ± 14.2	32.9 ± 6.1	31.3 ± 1.1		65.5 ± 6.3
4-6	27.1 ± 18.1	30.1 ± 6.0		57.2 ± 14.2	38.7 ± 4.7	33.5 ± 0.8		73.5 ± 5.3
6-12	40.6 ± 7.3	32.8 ± 6.3		73.4 ± 3.8				
12-24	50.0 ± 8.7	34.4 ± 6.7	0.55 ± 0.25	82.0 ± 4.2				

[a]Values are mean ± SD for four animals. See data for individual animals in Tables A4 - A7 in Appendix.

[b]Values are mean ± SD for three animals. See data for individual animals in Table A8 in Appendix.

[c]Part of the 1 h and 4 h urine samples were lost for some animals. Therefore actual cumulative values are somewhat higher than shown.

[d]Feces not analyzed.

[e]Feces analyzed as one combined sample, 0-72 h.

[f]Values are for excretion in breath as CO_2. Excretion in breath as volatiles was 0.82 ± 0.47 for 0-1 h, and 1.3 ± 0.8 for 1-2 h collection.

Table 7

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)[a]

Dose (mg/kg)	2.8				2.9			
Vehicle	10% Ethanol				2% Ethanol			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)								
0-1	0.42 ± 0.85	14.6 ± 3.1	N/A[b]	15.0 ± 2.9	2.5 ± 5.0	16.4 ± 1.9	N/A[b]	18.9 ± 5.5
1-2	5.0 ± 10.0	22.4 ± 3.4	N/A	27.4 ± 7.3	13.5 ± 15.1	22.4 ± 3.9	N/A	35.9 ± 18.7
2-4	21.9 ± 17.6	27.7 ± 5.1	N/A	49.5 ± 14.2	28.8 ± 8.4	27.8 ± 2.0	N/A	56.5 ± 9.3
4-6	27.1 ± 18.1	30.1 ± 6.0	N/A	57.2 ± 14.2	33.8 ± 6.4	30.6 ± 2.6	N/A	63.2 ± 7.2
6-12	40.6 ± 7.3	32.8 ± 6.3	N/A	73.4 ± 3.8	38.2 ± 5.8	32.4 ± 1.4	N/A	70.6 ± 6.1
12-24	50.0 ± 8.7	34.4 ± 6.7	0.55 ± 0.25	82.0 ± 4.2	45.2 ± 5.3	35.8 ± 1.0	0.5 ± 0.1	81.4 ± 5.2

[a]Values are mean ± SD for four animals. See data for individual animals in Tables A5 - A6.

[b]Feces analyzed as one combined sample, 0-72 h.

Table 8

Amount of ^{14}C-Labeled Compounds in Tissues 24 h After Intravenous Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats[a]

Dose (mg/kg)	2.8			2.9		
Dose Vehicle	10% EtOH/H_2O			2% EtOH/H_2O		
Tissue	ng-eq Cmpd per g Tissue	TRB[d]	% Dose	ng-eq Cmpd per g Tissue	TRB[d]	% Dose
I. Blood	606 ± 149	1.0 ± 0	1.4 ± 0.3	782 ± 112	1.0 ± 0	1.7 ± 0.3
II. Major Tissues						
Skin - Ear	344 ± 71	0.62 ± 0.31		344 ± 51	0.44 ± 0.03	
Neck	310 ± 105	0.57 ± 0.36		295 ± 39	0.38 ± 0.07	
Abdomen	342 ± 160	0.64 ± 0.48		413 ± 81	0.53 ± 0.06	
Hindquarters	388 ± 87	0.70 ± 0.36		406 ± 35	0.53 ± 0.11	
Average	346 ± 106	0.63 ± 0.38	1.9 ± 0.6	364 ± 39	0.47 ± 0.06	1.9 ± 0.2
Muscle - Neck	191 ± 25	0.32 ± 0.06		218 ± 39	0.28 ± 0.08	
Abdomen	149 ± 9	0.26 ± 0.09		179 ± 23	0.23 ± 0.03	
Hindleg	159 ± 12	0.27 ± 0.05		159 ± 10	0.20 ± 0.02	
Average	166 ± 10	0.28 ± 0.07	3.0 ± 0.1	185 ± 15	0.24 ± 0.04	3.2 ± 0.3
Adipose - Kidney	147 ± 23	0.25 ± 0.04		236 ± 71	0.30 ± 0.05	
Epididymis	109 ± 27	0.19 ± 0.07		157 ± 74	0.20 ± 0.09	
Mesenteric	208 ± 79	0.35 ± 0.13		433 ± 190	0.54 ± 0.16	
Average	155 ± 41	0.26 ± 0.08	0.56 ± 0.13	276 ± 104	0.34 ± 0.09	0.97 ± 0.38
Liver	456 ± 46	0.80 ± 0.28	0.68 ± 0.07	537 ± 53	0.70 ± 0.16	0.77 ± 0.09

(continued)

Table 8 (continued)

Amount of ^{14}C-Labeled Compounds in Tissues 24 h After Intravenous Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats[a]

Dose (mg/kg)	2.8			2.9		
Dose Vehicle	10% EtOH/H_2O			2% EtOH/H_2O		
Tissue	ng-eq Cmpd per g Tissue	TRB[d]	% Dose	ng-eq Cmpd per g Tissue	TRB[d]	% Dose
III. GI Tract Tissues						
Esophagus	533 ± 86	0.90 ± 0.19	0.014 ± 0.002	939 ± 399	1.2 ± 0.66	0.030 ± 0.010
Stomach	385 ± 61	0.68 ± 0.30	0.058 ± 0.010	386 ± 83	0.49 ± 0.05	0.071 ± 0.013
Small Intestine	490 ± 87	0.87 ± 0.41	0.22 ± 0.06	445 ± 68	0.57 ± 0.04	0.19 ± 0.04
Cecum	268 ± 116	0.50 ± 0.36	0.033 ± 0.007	278 ± 26	0.36 ± 0.02	0.042 ± 0.004[c]
Large Intestine	542 ± 113	0.96 ± 0.40	0.083 ± 0.016	579[c]	0.63[c]	0.077[c]
IV. Reproductive Tissues						
Testes	176 ± 30	0.31 ± 0.14	0.068 ± 0.012	172 ± 18	0.22 ± 0.03	0.062 ± 0.008
Seminal Vesicles	315 ± 46	0.56 ± 0.24	0.034 ± 0.006	316 ± 12	0.41 ± 0.05	0.027 ± 0.012
Prostate	415 ± 46	0.73 ± 0.29	0.014 ± 0.002	344 ± 128	0.44 ± 0.16	0.015 ± 0.005
V. Other Tissues						
Trachea	916 ± 118	1.5 ± 0.2	0.019 ± 0.006	1059 ± 357	1.3 ± 0.26	0.019 ± 0.010
Lungs	921 ± 76	1.6 ± 0.3	0.15 ± 0.01	974 ± 99	1.2 ± 0.2	0.16 ± 0.01
Adrenals	609 ± 82	1.1 ± 0.4	0.0065 ± 0.0012	816 ± 114	1.0 ± 0.01	0.0074 ± 0.0007
Spleen	612 ± 73	1.0 ± 0.3	0.044 ± 0.006	632 ± 83	0.81 ± 0.04	0.051 ± 0.012
Kidneys	421 ± 89	0.75 ± 0.38	0.12 ± 0.02	432 ± 68	0.55 ± 0.06	0.12 ± 0.02
Eyes	163 ± 41	0.29 ± 0.16[b]	0.0067 ± 0.0023[b]	223 ± 33	0.29 ± 0.06	0.0084 ± 0.0009
Brain	282 ± 126[b]	0.50 ± 0.08[b]	0.073 ± 0.029[b]	343 ± 29[b]	0.44 ± 0.06[b]	0.085 ± 0.008
Heart	340 ± 84[b]	0.60 ± 0.06[b]	0.039 ± 0.011[b]	320 ± 17[b]	0.40 ± 0.05[b]	0.035 ± 0.0004[b]

[a]Values are mean ± SD for 3 animals. See data for individual animals in Tables A27 - A29 and A33 - A35 in Appendix.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

[d]Tissue:blood ratio.

Table 9

Concentration of ^{14}C-Labeled Compounds in Tissues 72 h After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

Dose (mg/kg)	35	0.67
I. Blood	2350 ± 180	42 ± 7
II. Major Tissues		
Skin - Ear	4680 ± 350	86 ± 8
Neck	2190 ± 450	98 ± 25
Abdomen	3180 ± 500	65 ± 31
Hindquarters	2790 ± 1000	54 ± 13
Average	3210 ± 300	76 ± 16
Muscle - Neck	1510 ± 70	37 ± 10
Abdomen	910 ± 150	25 ± 5
Hindquarters	990 ± 230	22 ± 9
Average	1140 ± 100	28 ± 8
Adipose - Kidney	1470 ± 450	15 ± 6[b]
Epididymis	1120 ± 190	20 ± 2
Mesenteric	2660 ± 710	46 ± 5
Average	1750 ± 320	25 ± 5
Liver	6790 ± 1200	281 ± 113
III. GI Tract Tissues		
Esophagus	7030 ± 550	189 ± 62
Stomach	9220 ± 1430	570 ± 209
Small Intestine	4680 ± 810	32 ± 7
Cecum	2190 ± 610	12 ± 10
Large Intestine	3620 ± 170	30 ± 19
IV. Reproductive Tissues		
Testes	2280 ± 780	29 ± 6
Seminal Vesicles	3360 ± 730	60 ± 8
Prostrate	3250 ± 110	54 ± 4
V. Other Tissues		
Trachea	4650 ± 1640	98 ± 22
Lungs	4390 ± 1730	67 ± 7
Adrenals	10800 ± 120	138 ± 1
Spleen	4700 ± 290	74 ± 6
Kidneys	4730 ± 180	69 ± 6
Eyes	1190 ± 10[b]	20 ± 2
Brain	2230 ± 90	30 ± 9
Heart	2360[c]	46 ± 14

[a]Values are mean ± SD for 3 animals. See Tables A9 - A14 for data from individual animals.

[b]Mean ± range for 2 animals.

[c]Value for 1 animal.

Table 10

Tissue-Blood Ratios of ^{14}C-Labeled Compounds After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Dose (mg/kg)		35	0.67
I.	Blood	1.0 ± 0.0	1.0 ± 0.0
II.	Major Tissues		
	Skin - Ear	2.0 ± 0.1	2.1 ± 0.2
	Neck	0.94 ± 0.25	2.3 ± 0.6
	Abdomen	1.3 ± 0.1	1.5 ± 0.4
	Hindquarters	1.2 ± 0.5	1.3 ± 0.1
	Average	1.4 ± 0.2	1.8 ± 0.2
	Muscle - Neck	0.64 ± 0.03	0.87 ± 0.12
	Abdomen	0.39 ± 0.08	0.60 ± 0.02
	Hindleg	0.42 ± 0.06	0.50 ± 0.12
	Average	0.48 ± 0.03	0.66 ± 0.08
	Adipose - Kidney	0.62 ± 0.15	0.36 ± 0.20[b]
	Epididymis	0.48 ± 0.11	0.48 ± 0.08
	Mesenteric	1.1 ± 0.3	1.1 ± 0.3
	Average	0.75 ± 0.14	0.61 ± 0.16
	Liver	2.9 ± 0.5	7.1 ± 3.5
III.	GI Tract Tissues		
	Esophagus	3.0 ± 0.2	4.4 ± 1.0
	Stomach	3.9 ± 0.6	14 ± 5
	Small Intestine	2.0 ± 0.3	0.76 ± 0.02
	Cecum	0.94 ± 0.28	0.27 ± 0.19
	Large Intestine	1.5 ± 0.1	0.68 ± 0.31
IV.	Reproductive Tissues		
	Testes	0.98 ± 0.35	0.69 ± 0.03
	Seminal Vesicles	1.4 ± 0.3	1.4 ± 0.05
	Prostate	1.4 ± 0.1	1.3 ± 0.1
V.	Other Tissues		
	Trachea	2.0 ± 0.7	2.3 ± 0.1
	Lungs	1.8 ± 0.6	1.6 ± 0.1
	Adrenals	4.6 ± 0.3	3.4 ± 0.6
	Spleen	2.0 ± 0.1	1.8 ± 0.1
	Kidneys	2.0 ± 0.2	1.7 ± 0.1
	Eyes	0.49 ± 0.03[b]	0.48 ± 0.03
	Brain	0.95 ± 0.04	0.70 ± 0.08
	Heart	0.92[c]	1.1 ± 0.1

[a]Values are the mean for 3 rats ± SD. See Tables A9 - A14 for data from individual animals.

[b]Mean ± range for 2 animals.

[c]Value for 1 animal.

Table 11

Amount of ^{14}C-Labeled Compounds in Tissues 72 h After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Dose (mg/kg)		35	0.67
I.	Blood	0.43 ± 0.1	0.41 ± 0.06
II.	Major Tissues		
	Skin	1.4 ± 0.2	1.8 ± 0.3
	Muscle	1.6 ± 0.1	2.2 ± 0.5
	Adipose	0.51 ± 0.10	0.39 ± 0.07
	Liver	0.66 ± 0.12	1.5 ± 0.7
III.	GI Tract Tissues		
	Esophagus	0.017 ± 0.001	0.022 ± 0.004
	Stomach	0.16 ± 0.03	0.83 ± 0.20
	Small Intestine	0.13 ± 0.01	0.10 ± 0.02
	Cecum	0.022 ± 0.005	0.021 ± 0.008
	Large Intestine	0.041 ± 0.003	0.034 ± 0.004
IV.	Reproductive Tissues		
	Testes	0.070 ± 0.026	0.046 ± 0.003
	Seminal Vesicles	0.018 ± 0.005	0.020 ± 0.002
	Prostate	0.012 ± 0.006	0.010 ± 0.003
V.	Other Tissues		
	Trachea	0.0097 ± 0.0038	0.0099 ± 0.0022
	Lungs	0.044 ± 0.009	0.040 ± 0.003
	Adrenals	0.0043 ± 0.0008	0.0047 ± 0.0007
	Spleen	0.027 ± 0.001	0.022 ± 0.003
	Kidneys	0.094 ± 0.005	0.080 ± 0.007
	Eyes	0.0032 ± 0.0004[b]	0.0032 ± 0.0003
	Brain	0.041 ± 0.002	0.030 ± 0.008
	Heart	0.018[c]	0.023 ± 0.010

[a]Values are mean ± SD for 3 animals.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

[d]Adipose assumed to be 10% of body weight; muscle, 50% of body weight; and skin, 15% of body weight.

Table 12

Concentration of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

	Time (h)	0.25	0.75	2	6	24	72
I.	Blood	11400 ± 100	5820 ± 630	2370 ± 70	950 ± 88	606 ± 149	371 ± 96
II.	Major Tissues						
	Skin - Ear	1200 ± 80	1010 ± 32	516 ± 14	383 ± 23	344 ± 71	264 ± 29
	Neck	1180 ± 50	1070 ± 100	482 ± 92	325 ± 102	310 ± 105	193 ± 66
	Abdomen	1430 ± 90	1260 ± 150	731 ± 187	368 ± 70	342 ± 160	182 ± 36
	Hindquarters	927 ± 139	954 ± 36	692 ± 65	403 ± 2[b]	388 ± 87	196 ± 5
	Average	1160 ± 60	1070 ± 19	605 ± 32	366 ± 12	346 ± 106	209 ± 28
	Muscle - Neck	1190 ± 20	839 ± 71	385[c]	228 ± 56	191 ± 25	122 ± 19
	Abdomen	974 ± 158[b]	746 ± 57	382 ± 47	230 ± 18	149 ± 9	133 ± 27
	Hindquarters	910 ± 24	750 ± 44	357 ± 34	156 ± 23	159 ± 12	98 ± 11
	Average	1030 ± 40	778 ± 52	376 ± 29	205 ± 28	166 ± 10	118 ± 19
	Adipose - Kidney	248 ± 94	136 ± 26	99 ± 41[b]	94 ± 27	147 ± 23	55 ± 8
	Epididymis	263 ± 92	284 ± 196	109 ± 27	99 ± 40	109 ± 27	70 ± 23
	Mesenteric	733 ± 266	394 ± 153	281 ± 72	264 ± 66	208 ± 79	144 ± 35
	Average	414 ± 133	271 ± 69	176 ± 52	153 ± 37	155 ± 41	90 ± 20
	Liver	4150 ± 147	3490 ± 130	2120 ± 288	937 ± 147	456 ± 46	293 ± 25
III.	GI Tract Tissues						
	Esophagus	N/A	N/A	N/A	747 ± 139	533 ± 86	N/A
	Stomach	N/A	N/A	N/A	663 ± 56	385 ± 61	N/A
	Small Intestine	N/A	N/A	N/A	1240 ± 238	490 ± 87	N/A
	Cecum	N/A	N/A	N/A	695 ± 205	268 ± 116	N/A
	Large Intestine	N/A	N/A	N/A	995 ± 90	542 ± 113	N/A

(continued)

Table 12 (continued)

Concentration of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

Time (h)	0.25	0.75	2	6	24	72
IV. Reproductive Tissues						
Testes	N/A	N/A	N/A	303 ± 43	176 ± 30	N/A
Seminal Vesicles	N/A	N/A	N/A	284 ± 180[b]	315 ± 46	N/A
Prostate	N/A	N/A	N/A	728 ± 241[b]	415 ± 46	N/A
V. Other Tissues						
Trachea	N/A	N/A	N/A	1190 ± 240	916 ± 118	461 ± 63
Lungs	N/A	N/A	N/A	1410 ± 270	921 ± 76	504 ± 39
Adrenals	N/A	N/A	N/A	779 ± 42	609 ± 82	536 ± 70
Spleen	N/A	N/A	N/A	944 ± 36	612 ± 73	N/A
Kidneys	N/A	N/A	N/A	856 ± 79	421 ± 89	N/A
Eyes	N/A	N/A	N/A	247 ± 21[b]	163 ± 41[b]	N/A
Brain	N/A	N/A	N/A	631 ± 55[b]	282 ± 126[b]	N/A
Heart	N/A	N/A	N/A	568 ± 35	340 ± 84[b]	N/A

[a]Values are mean ± SD for 3 animals. See Tables A15 - A32 for individual animal data.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

Table 13

Tissue Blood Ratios of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Time (h)	0.25	0.75	2	6	24	72
I. Blood	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0
II. Major Tissues						
Skin - Ear	0.10 ± 0.01	0.17 ± 0.02	0.22 ± 0.002	0.40 ± 0.03	0.62 ± 0.31	0.76 ± 0.31
Neck	0.10 ± 0.01	0.18 ± 0.03	0.20 ± 0.03	0.35 ± 0.13	0.57 ± 0.36	0.54 ± 0.17
Abdomen	0.12 ± 0.01	0.22 ± 0.02	0.31 ± 0.08	0.39 ± 0.06	0.64 ± 0.48	0.51 ± 0.14
Hindquarters	0.08 ± 0.01	0.16 ± 0.01	0.29 ± 0.02	0.43 ± 0.05[b]	0.70 ± 0.36	0.55 ± 0.15
Average	0.10 ± 0.01	0.18 ± 0.02	0.26 ± 0.02	0.39 ± 0.04	0.63 ± 0.38	0.59 ± 0.18
Muscle - Neck	0.10 ± 0.002	0.14 ± 0.02	0.17[c]	0.24 ± 0.08	0.32 ± 0.06	0.34 ± 0.08
Abdomen	0.08 ± 0.01[b]	0.13 ± 0.01	0.16 ± 0.02	0.24 ± 0.04	0.26 ± 0.09	0.37 ± 0.10
Hindquarters	0.080 ± 0.002	0.13 ± 0.02	0.15 ± 0.01	0.17 ± 0.04	0.27 ± 0.05	0.28 ± 0.08
Average	0.091 ± 0.004	0.13 ± 0.02	0.16 ± 0.01	0.22 ± 0.05	0.28 ± 0.07	0.33 ± 0.09
Adipose - Kidney	0.022 ± 0.008	0.023 ± 0.002	0.043 ± 0.019[b]	0.10 ± 0.03	0.25 ± 0.04	0.16 ± 0.07
Epididymis	0.023 ± 0.008	0.047 ± 0.027	0.046 ± 0.012	0.10 ± 0.04	0.19 ± 0.07	0.20 ± 0.08
Mesenteric	0.064 ± 0.024	0.068 ± 0.028	0.12 ± 0.03	0.28 ± 0.07	0.35 ± 0.13	0.42 ± 0.22
Average	0.036 ± 0.012	0.046 ± 0.008	0.074 ± 0.022	0.16 ± 0.04	0.26 ± 0.08	0.26 ± 0.12
Liver	0.36 ± 0.01	0.60 ± 0.08	0.89 ± 0.11	1.0 ± 0.2	0.80 ± 0.28	0.84 ± 0.32
III. GI Tract Tissues						
Esophagus	N/A	N/A	N/A	0.79 ± 0.17	0.90 ± 0.19	N/A
Stomach	N/A	N/A	N/A	0.70 ± 0.01	0.68 ± 0.30	N/A
Small Intestine	N/A	N/A	N/A	1.3 ± 0.2	0.87 ± 0.41	N/A
Cecum	N/A	N/A	N/A	0.73 ± 0.17	0.50 ± 0.36	N/A
Large Intestine	N/A	N/A	N/A	1.0 ± 0.02	0.96 ± 0.40	N/A

(continued)

Table 13 (continued)

Tissue Blood Ratios of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Time (h)	0.25	0.75	2	6	24	72
IV. Reproductive Tissues						
Testes	N/A	N/A	N/A	0.32 ± 0.02	0.31 ± 0.14	N/A
Seminal Vesicles	N/A	N/A	N/A	0.31 ± 0.22[b]	0.56 ± 0.24	N/A
Prostate	N/A	N/A	N/A	0.80 ± 0.21[b]	0.73 ± 0.29	N/A
V. Other Tissues						
Trachea	N/A	N/A	N/A	1.2 ± 0.2	1.5 ± 0.2	1.3 ± 0.2
Lungs	N/A	N/A	N/A	1.5 ± 0.4	1.6 ± 0.3	1.4 ± 0.4
Adrenals	N/A	N/A	N/A	0.82 ± 0.04	1.1 ± 0.4	1.5 ± 0.5
Spleen	N/A	N/A	N/A	1.0 ± 0.05	1.0 ± 0.2	N/A
Kidneys	N/A	N/A	N/A	0.90 ± 0.07	0.75 ± 0.38	N/A
Eyes	N/A	N/A	N/A	0.26 ± 0.01[b]	0.29 ± 0.16[b]	N/A
Brain	N/A	N/A	N/A	0.66 ± 0.03[b]	0.50 ± 0.08[b]	N/A
Heart	N/A	N/A	N/A	0.60 ± 0.05	0.60 ± 0.06[b]	N/A

[a]Values are mean ± SD for 3 animals. See Tables A15 - A32 for individual animal data.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

Table 14

Amount of ^{14}C-Labeled Compound in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Time (h)	0.25	0.75	2	6	24	72
I. Blood	25 ± 0.3	13 ± 2	5.1 ± 0.12	2.3 ± 0.2	1.4 ± 0.3	0.83 ± 0.19
II. Major Tissues						
Skin	6.0 ± 0.3	5.6 ± 0.2	3.1 ± 0.2	2.1 ± 0.1	1.9 ± 0.6	1.1 ± 0.2
Muscle	18 ± 0.7	14 ± 1	6.4 ± 0.5	4.0 ± 0.6	3.0 ± 0.1	2.1 ± 0.4
Adipose	1.4 ± 0.5	0.95 ± 0.26	0.60 ± 0.17	0.59 ± 0.14	0.56 ± 0.13	0.32 ± 0.08
Liver	5.0 ± 0.3	3.8 ± 0.3	2.8 ± 0.6	1.3 ± 0.2	0.68 ± 0.07	0.38 ± 0.04
III. GI Tract Tissues						
Esophagus	N/A	N/A	N/A	0.027 ± 0.007	0.014 ± 0.002	N/A
Stomach	N/A	N/A	N/A	0.11 ± 0.01	0.058 ± 0.010	N/A
Small Intestine	N/A	N/A	N/A	0.52 ± 0.08	0.22 ± 0.06	N/A
Cecum	N/A	N/A	N/A	0.071 ± 0.011	0.033 ± 0.007	N/A
Large Intestine	N/A	N/A	N/A	0.19 ± 0.02	0.083 ± 0.016	N/A
IV. Reproductive Tissues						
Testes	N/A	N/A	N/A	0.12 ± 0.01	0.068 ± 0.012	N/A
Seminal Vesicles	N/A	N/A	N/A	0.032 ± 0.017	0.034 ± 0.006	N/A
Prostate	N/A	N/A	N/A	0.026 ± 0.010[b]	0.014 ± 0.002	N/A

(continued)

Table 14 (continued)

Amount of ^{14}C-Labeled Compound in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Time (h)	0.25	0.75	2	6	24	72
V. Other Tissues						
Trachea	N/A	N/A	N/A	0.026 ± 0.004	0.019 ± 0.006	0.011 ± 0.002
Lungs	N/A	N/A	N/A	0.24 ± 0.06	0.15 ± 0.01	0.074 ± 0.002
Adrenals	N/A	N/A	N/A	0.0066±0.0014	0.0065±0.0012	0.0027±0.0010
Spleen	N/A	N/A	N/A	0.072 ± 0.013	0.044 ± 0.006	N/A
Kidneys	N/A	N/A	N/A	0.25 ± 0.03	0.12 ± 0.02	N/A
Eyes	N/A	N/A	N/A	0.011 ± 0	0.0067 ± 0.002[b]	N/A
Brain	N/A	N/A	N/A	0.13 ± 0.02[b]	0.073 ± 0.029[b]	N/A
Heart	N/A	N/A	N/A	0.068 ± 0.003	0.039 ± 0.011[b]	N/A

[a]Values are mean ± SD for 3 animals. See Tables A15 - A32 for individual animal data.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

APPENDIX

Figure A1. Data Sheets for [^{14}C]Crotonaldehyde Supplied by MRI

SHIPPING ORDER

MIDWEST RESEARCH INSTITUTE

425 Volker Boulevard, Kansas City, Missouri 64110

№ 55050

☐ SALE
☒ TRANSFER
☐ RETURN FOR CREDIT
☐ EXCHANGE

REFER TO THIS NO. IN ALL CORRESPONDENCE

DATE 8/1/83

TO [redacted], Research Triangle Institute, Research Triangle Park, NC 27709

VIA			
Federal Express 287463610	☐ COLLECT ☒ PREPAID	INSURE: ☐ YES ☒ NO AMOUNT	
REQUESTED BY	CHARGE	REFERENCE	
[redacted]	7543-C-1		

QUANTITY	DESCRIPTION OF MATERIAL	PRESENT LOCATION
2X72 mg.	[U-14C]Crotonaldehyde	
	at 2.31 mCi/mmole in 0.65 mls. of water	
2X2.365 mCi	Lot #: 83-127-16-30	

[redacted]

PACKING SLIP

MRI 11 REV 11-68

Figure A1. (continued)

MIDWEST RESEARCH INSTITUTE
425 Volker Boulevard
Kansas City, Missouri 64110
Telephone (816) 753-7600

ANALYTICAL DATA SUMMARY

MRI Project No. 7543-C(1)

COMPOUND: [U-^{14}C]-Crotonaldehyde

FORMULA: C_4H_6O

STRUCTURE: $CH_3CH{=}CHCHO$ (* * * *)

LOT NO.: 83-127-16-30

AMOUNT: 4.73 mCi (2 x 2.365 mCi)

SPECIFIC ACTIVITY: 2.31 mCi/mM

ESTIMATED PURITY: $\geq$ 99%, chemical and radiochemical (GLC)

FORM SUPPLIED: 2 x (2.365 mCi in 0.65 ml water) in 2-ml amber ampules under argon

GLC ANALYSIS: 20% SP-2100 w/0.1% Carbowax

Oven Temperature: 50° isothermal
Injector Temperature: 250°
Detector Temperature: 250° FID
Carrier Gas: 40 ml argon/min
Detector Gas: H_2, 30 ml/min
Air, 300 ml/min
Retention Time: Crotonaldehyde, 8.9 min
Injection Solvent: Ether (conc. $\sim 1 \times 10^{-1}$ mM/ml)
Traces attached

STORAGE AND HANDLING RECOMMENDATIONS: Store at $\leq$ 0°C in dark, open only in a well-ventilated hood

Figure A1. (continued)

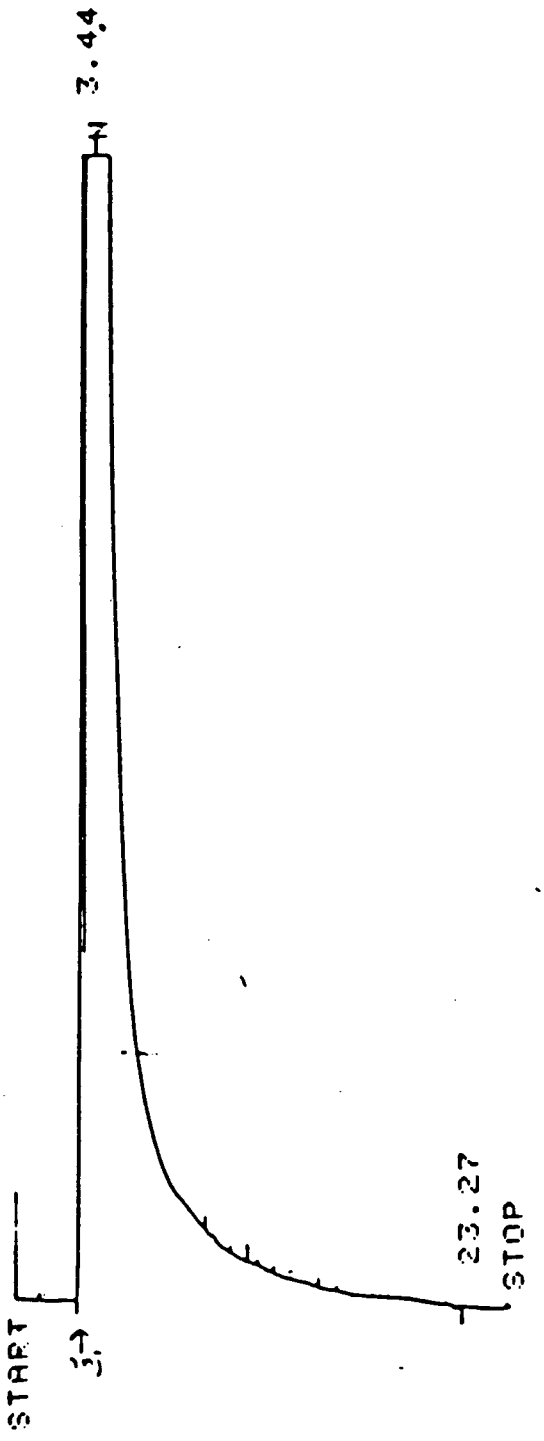


Figure 1 - GLC of Ether Sample Solvent (20% SP-2100 w/0.1% Carbowax; 50° Isothermal); RT Ether ∿ 3.4 min

Figure A1. (continued)

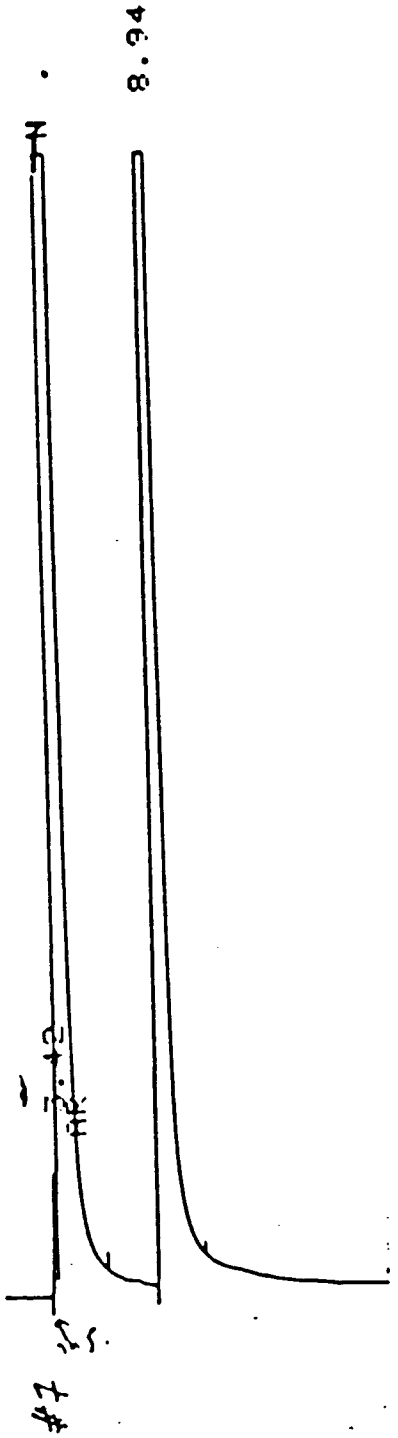


Figure 2 - GLC of Crotonaldehyde (Eastman) in Ether Solvent, RT Crotonaldehyde 8.9 min; Conditions Same as Figure 1

Figure A1. (continued)

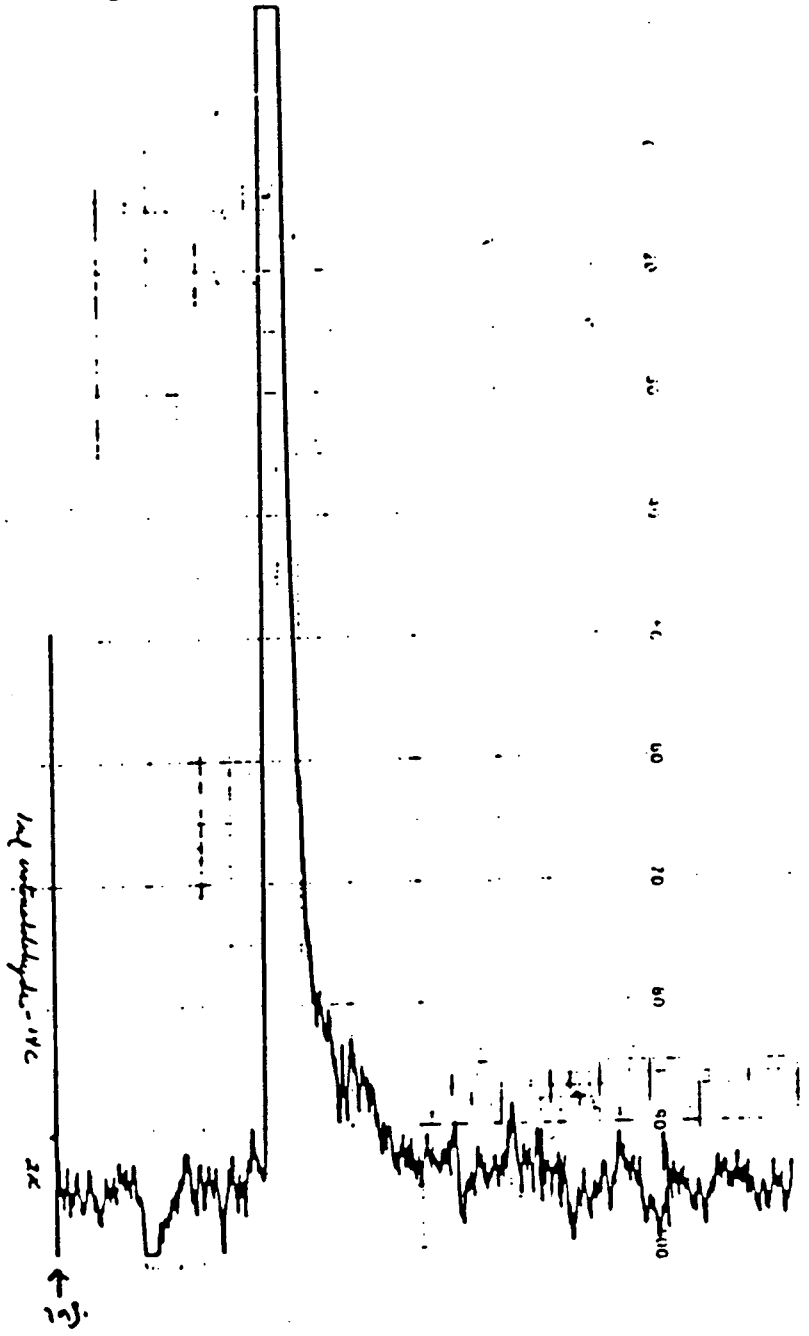


Figure 3 - Radio GLC of [U-^{14}C]-Crotonaldehyde, Lot No. 83-127-16-30 in Ether Solvent; Conditions Same as Figure 1

Figure A1. (continued)

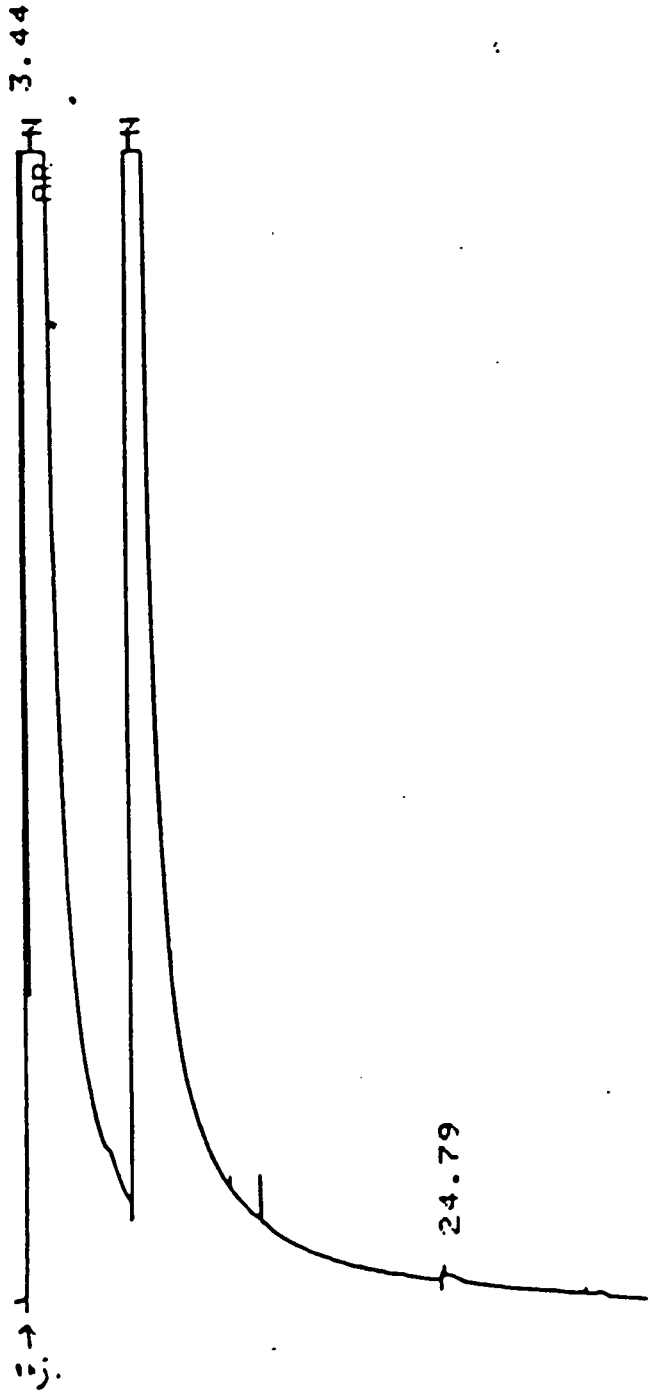


Figure 4 - Mass GLC of [U-^{14}C]-Crotonaldehyde, Lot No. 83-127-16-30 in Ether Solvent; Conditions Same as Figure 1

Figure A1. (continued)

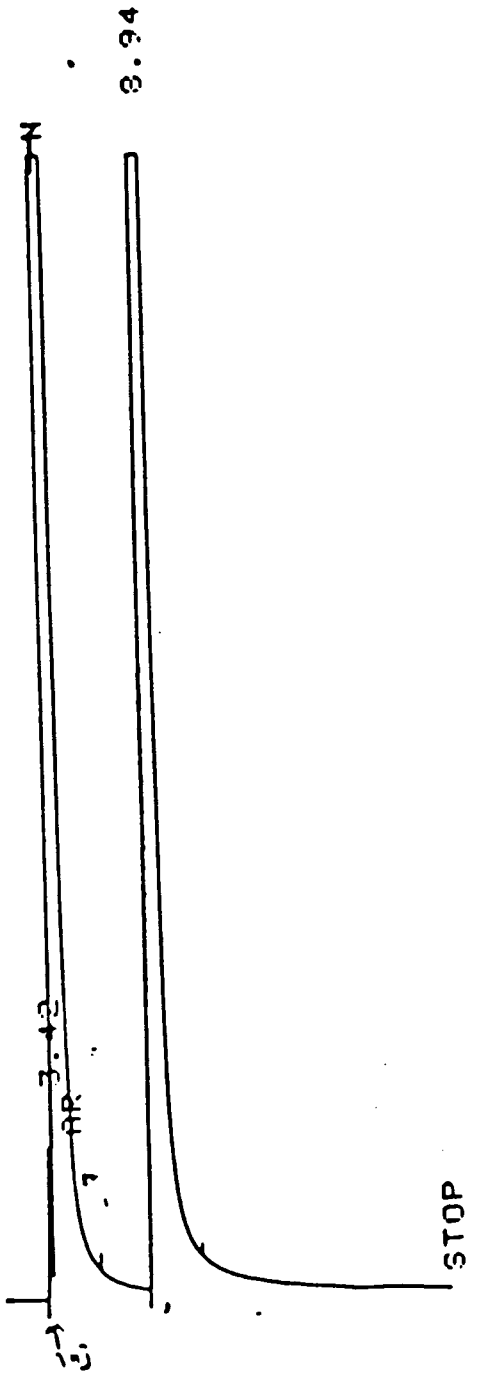


Figure 5 - Mass GLC of Coinjection of [U-^{14}C]-Crotonaldehyde, Lot No. 83-127-16-30 and Crotonaldehyde (Eastman) in Ether Solvent; Conditions Same as Figure 1

Table A1

Cumulative Excretion of Total ^{14}C After Oral Administration of 0.67 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Rat	4188-121-5				4188-121-6				4188-121-7			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)												
12	39.3	37.4	a	76.7	40.1	46.1	a	86.2	31.6	39.4	a	71.0
24	40.8	b	7.2	85.4	41.2	48.4	4.8	94.4	34.2	41.0	5.2	80.4
36	41.1	41.7[b]		90.0	41.6	50.3		96.7	34.4	42.9		82.5
48	41.2	42.5	7.4	91.1	41.7	51.1	5.7	98.5	34.5	43.5	6.1	84.1
72	41.5	43.3	7.6	92.4	42.1	52.6	5.8	100.5	34.7	44.5	6.3	85.5

[a]The first feces collection was 0-24 h.

[b]The 12-24 h and the 24-36 h breath samples were accidentally combined before analysis. The percent dose excreted for this combined sample is recorded as one sample, 24-36 h.

Table A2

Cumulative Excretion of Total ^{14}C After Oral Administration of 3.3 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Rat	4188-121-2				4188-121-3				4188-121-4			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)												
12	33.9	46.9	a	80.8	26.0	36.1	a	62.1	31.8	48.5	a	80.3
24	35.2	b	2.8	84.9	30.6	b	9.4	76.1	32.8	b	3.2	84.5
36	35.4	48.4		86.6	31.0	37.7		78.1	33.2	50.1		86.5
48	35.4	51.0[b]	3.2	89.6	31.2	40.2[b]	9.8	81.2	33.3	52.6[b]	3.4	89.3
72	35.6	52.4	3.3	91.3	32.3	41.1	10.0	83.4	34.1	53.7	3.5	91.3

[a]The first feces collection was 0-24 h.

[b]The 12-24 h and the 36-48 h breath samples were accidentally combined before analysis. The percent dose excreted for this combined sample is recorded as one sample, 36-48 h.

Table A3

Cumulative Excretion of Total ^{14}C After Oral Administration of 35 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Rat	4188-77-1[a]					4188-77-2					4188-77-3					4188-77-4				
Excreta	Urine	Breath CO_2	Breath volatiles	Feces	Total	Urine	Breath CO_2	Breath volatiles	Feces	Total	Urine	Breath CO_2	Breath volatiles	Feces	Total	Urine	Breath CO_2	Breath Volatiles	Feces	Total
Time (h)																				
12	20	28	0.47	b	49	34	38	0.26	b	73	36	29	0.097	b	65	17	34	0.12	b	51
24	30	38	0.51	0	69	38	42	0.28	5.7	86	39	33	0.10	4.5	76	33	41	0.13	1.6	76
36	34	44	0.52		79	39	43	0.28		88	40	35	0.11		79	34	43	0.14		79
48	35	46		4.7	87	39	44		6.2	89	41	36		6.8	84	35	44		4.7	84
72	35	48		7.0	91	40	45		6.6	92	41	36		6.9	85	35	45		7.2	87

[a]This animal was not used in tissue data compilation.

[b]The first feces collection was 0-24 h.

Table A4

Cumulative Excretion of Total ^{14}C After Intravenous Administration of 2.6 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Animal	4188-178-1				4188-178-2				4188-178-3				4188-178-4			
Excreta	Urine	Breath (CO_2)	Breath (volatiles)	Total	Urine	Breath (CO_2)	Breath (volatiles)	Total	Urine	Breath (CO_2)	Breath (volatiles)	Total	Urine	Breath (CO_2)	Breath (volatiles)	Total
Time (h)																
0-1	0.0	18.9	0.5	19.4	3.8	10.5	1.5	15.8	20.8	17.5	0.8	39.1	17.2	18.6	0.5	36.3
1-2	0.2	24.6	0.9	25.7	27.4	21.8	2.4	51.6	21.0	25.6	1.0	47.6	17.7	26.0	0.8	44.5
2-4	27.9	30.8		59.6	34.0	30.0		66.4	28.6	32.4		62.0	41.1	32.0		73.9
4-6	33.7	32.7		67.3	40.4	33.0		75.8	36.3	34.1		71.4	44.4	34.3		79.5

Table A5

Cumulative Excretion of Total ^{14}C After Intravenous Administration of 2.8 mg/kg [^{14}C]Crotonaldehyde in a Vehicle of 10% Aqueous Ethanol to Male Fischer 344 Rats (% Dose)

Animal	4188-151-1				4188-151-2				4188-151-3				4188-151-4			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)																
0-1	0	17.9		17.9	0	11.1		11.1	1.7	12.8		14.5	0	16.4		16.4
1-2	0	26.4		26.4	0	23.1		23.1	20.0	18.0		38.0	0	22.2		22.2
2-4	0	33.6		33.6	30.0	29.6		59.6	20.0	21.5		41.5	37.0	26.2		63.2
4-6	0	36.7		36.7	35.4	32.6		68.0	36.0	22.6		58.6	37.0	28.4		65.4
6-12	31.0	40.3		71.3	39.1	34.7		73.8	44.8	25.2		70.0	47.6	31.1		78.7
12-24	37.3	42.6	0.9	80.8	42.0	36.1	0.5	78.6	53.3	26.5	0.5	80.3	55.3	32.5	0.3	88.1

Table A6

Cumulative Excretion of Total ^{14}C After Intravenous Administration of 2.9 mg/kg [^{14}C]Crotonaldehyde in a Vehicle of 2% Aqueous Ethanol to Male Fischer 344 Rats (% Dose)

Animal	4188-152-1				4188-152-2				4188-152-3				4188-152-4			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)																
0-1	0	14.9		14.9	0	18.9		18.9	9.9	16.7		26.6	0	15.1		15.1
1-2	0	20.7		20.7	31.7	26.1		57.8	20.1	25.0		45.1	2.2	17.7		19.9
2-4	21.6	25.4		47.0	40.4	28.9		69.3	23.9	29.9		53.8	29.2	26.8		56.0
4-6	29.5	27.0		56.5	42.9	30.5		73.4	29.4	31.6		61.0	33.2	28.8		62.0
6-12	33.7	30.6		64.3	45.1	32.9		78.0	33.0	34.0		67.0	41.0	32.0		73.0
12-24	41.5	34.7	0.3	76.5	51.8	35.4	0.6	87.8	40.3	37.1	0.5	77.9	47.0	36.0	0.6	83.6

Table A7

Cumulative Excretion of Total ^{14}C After Intravenous Administration of 2.8 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Animal	4275-40-1				4275-40-2				4275-40-3				4275-40-4			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)																
0-1	0	18.0	a	18.0	7.6[b]	18.4	a	26.0	14.6[b]	14.3	a	28.9	15.6[b]	14.3	a	29.9
1-2	0	30.2		30.2	15.3	27.1		42.4	14.8	24.0		38.8	25.5	23.1		48.6
2-4	26.3[b]	37.8		64.1	17.7	31.5		49.2	15.0	29.8		44.8	32.4	28.8		61.2
4-6	26.8	40.8		67.6	17.8	33.8		51.6	33.1	31.9		65.0	38.0	31.0		69.0
6-12	33.6	43.7		77.3	29.6	36.5		66.1	42.3	35.5		77.8	40.7	33.7		74.4
12-24	34.8	46.1		80.9	31.6	38.1		69.7	43.9	37.7		81.6	41.6	35.1		76.7
24-36	35.4	47.1		82.5	32.1	39.2		71.3	44.4	38.8		83.2	41.9	36.1		78.0
36-48	35.7	48.0		83.7	32.3	39.9		72.2	44.6	39.4		84.0	42.1	36.7		78.8
48-72	36.2	49.2		85.4	32.6	40.8		73.4	44.9	40.4		85.3	42.4	37.5		79.9

[a]Feces were not analyzed.

[b]Urine sample was partially lost due to leaky joints in the metabolism cage.

Table A8

Cumulative Excretion of Total ^{14}C After Intravenous Administration of 2.8 mg/kg [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Animal	4275-130-1				4275-130-2				4275-130-4			
Excreta	Urine	Breath	Feces[a]	Total	Urine	Breath	Feces[a]	Total	Urine	Breath	Feces[a]	Total
Time (h)												
0-1	2.6	16.2		18.8	1.7	16.8		18.5	0	16.8		16.8
1-2	21.8	25.7		47.5	32.2	25.7		57.9	0	26.5		26.5
2-4	23.0	30.9		53.9	36.4	29.9		66.3	42.0[b]	32.5		
4-6	32.5	33.3		65.8	46.2	31.9		78.1		34.6		76.6
6-12	37.5	37.3		74.8	51.4	34.3		85.7	47.4	37.7		85.1
12-24	39.3	39.3		78.6	52.3	35.7		88.0	48.8	39.6		88.4
24-36	39.8	40.5		80.3	52.7	36.7		89.4	49.2	40.8		90.0
36-48	40.1	41.2		81.3	52.9	37.3		90.2	49.4	41.5		90.9
48-72	40.3	42.3	0.4	83.0	53.1	38.0	0.2	91.3	49.6	42.3	0.2	92.1

[a]Feces analyzed as one combined sample, 0-72 h.

[b]The 2-4 and 4-6 h samples were accidentally combined before analysis. The percent dose excreted for this combined sample is recorded as one sample.

Table A9. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 0.67 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-121-5

TISSUE ANALYSIS

STUDY ID: CROT-3 Length (hrs): 72 Route: ORAL Dose date: 09-06-83 (MM-DD-YY)

ANIMAL ID: 4188-121-5 YELLOW Rat Strain: F334 MALE Body Wt. (g) 281.0

DOSE Amt: .715 mg/kg
.201 mg Cmpd
1.3e7 dpm
Ref: 4188-127 Notebook-page for dose data.
Spec. Act: 73.2 dpm/ng 14C-Cmpd, ref. p. 4188-128

Vehicle: 10% ETOH

RTI Project 311-2227 File Name: CROT-3
Master Protocol 89 edited: 04108A-PP
Today's Date: 5/ 8/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2075	858.8	4139	3672	50.2	1.000	.478
	2			.2080	852.1	4097				
	3			.2634	900.2	3418				
	4			.3541	1074	3033				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1227	886.6	7226	6760	92.3	1.841	2.095
	2			.2035	1262	6294				
Neck	1	1	N/A	.2185	1695	7757	7757	106.0	2.113	2.404
	2			.0000	0	0				
Abdomen	1	1	N/A	.2080	1506	7240	7240	98.9	1.972	2.264
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.1991	1001	5028	5028	68.7	1.369	1.556
	2			.0000	0	0				
				AVERAGES FOR SKIN				91.5	1.824	2.075
MUSCLE:										
Neck	1	1	N/A	.5042	1739.4	3450	3450	47.1	.940	3.564
	2			.0000	0	0				
Abdomen	1	1	N/A	.6184	1389.2	2246	2246	30.7	.612	2.321
	2			.0000	0	0				
Hindleg	1	1	N/A	.4102	947.4	2310	2310	31.6	.629	2.386
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				36.5	.727	2.757
ADIPOSE:										
Kidney	1	1	N/A	.3768	295.2	783	783	10.7	.213	.162
	2			.0000	0	0				
Epididymis	1	1	N/A	.1650	240.3	1456	1456	19.9	.397	.301
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2971	879.6	2961	2961	40.4	.806	.612
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				23.7	.472	.358
LIVER:	1	4	7.7755	.3110	3551	11418	11419	156.0	3.110	.653
	2			.4150	4773	11501				
	3			.2750	3131	11385				
	4			.3280	3730	11372				
III. GI TRACT TISSUES										
Esophagus		1	.1945	.1945	3410	17532	17532	239.5	4.775	.025
Stomach	1	1	2.3331	2.3331	102745	44038	44038	601.6	11.994	.755
	2			.0000	0	0				
Sm. Intest	1	1	5.5675	5.5675	16050	2883	2883	39.4	.785	.118
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	2.2146	2.2146	3947	1782	1782	24.3	.485	.029
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.3129	1.3129	5013	3818	3818	52.2	1.040	.037
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.6288	2.6288	6719	2556	2556	34.9	.696	.049
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.5665	.5665	2855	5040	5040	68.8	1.373	.021
	2			.0000	0	0				
Prostate		1	.4372	.4372	1847	4225	4225	57.7	1.151	.014
V. OTHER TISSUES										
Trachea		1	.1814	.1814	1616	8908	8908	121.7	2.426	.012
Lungs	1	1	1.0825	1.0825	5987	5531	5531	75.6	1.506	.066
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0577	.0577	585	10139	10139	138.5	2.761	.006
Spleen	1	1	.4079	.4079	2434	5967	5967	81.5	1.625	.018
	2			.0000	0	0				
Kidneys	1	1	2.1462	2.1462	11820	5507	5507	75.2	1.500	.087
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2965	.2965	485	1636	1636	22.3	.446	.004
	2			.0000	0	0				
Brain	1	1	1.8953	1.8953	5338	2877	2877	39.3	.784	.039
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	1.0394	1.0394	4676	4499	4499	61.5	1.225	.034
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A10. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 0.67 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-121-6

TISSUE ANALYSIS

STUDY ID: CROT-3 Length (hrs): 72 Route: ORAL Dose date: 09-06-83 (MM-DD-YY)

ANIMAL ID: 4188-121-6 green Rat Strain: F334 MALE Body Wt. (g) 281.0

DOSE Amt: .663 mg/kg
.186 eq Cmpd
1.33e7 dpm
Ref: 4188-127 Notebook-page for dose data.
Spec. Act: 73.2 dpm/ng 14C-Cmpd, ref. p. 4188-128

Vehicle: 10% ETOH

RTI Project 310-2227 File Name: CROT-3
Master Protocol 89 edited: 041084-PP
Today's Date: 5/ 8/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.4301	1106	2571	2891	39.5	1.0000	.385
	2			.3387	1128	3330				
	3			.3308	971	2935				
	4			.3302	900	2726				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1535	999	6508	6410	87.6	2.2175	2.032
	2			.1082	683	6312				
Neck	1	1	N/A	.4421	3806	8609	8609	117.6	2.9781	2.728
	2			.0000	0	0				
Abdomen	1	1	N/A	.4182	1744	4170	4170	57.0	1.4426	1.322
	2			.0000	0	0				
Hindquarters	1	1	N/A	.3482	1158	3326	3326	45.4	1.1505	1.056
	2			.0000	0	0				
				AVERAGES FOR SKIN				76.9	1.9472	1.784
MUSCLE:										
Neck	1	1	N/A	.5434	1482	2727	2727	37.3	.9435	2.881
	2			.0000	0	0				
Abdomen	1	.1	N/A	.4915	863	1756	1756	24.0	.6074	1.855
	2			.0000	0	0				
Hindleg	1	1	N/A	.5719	795	1390	1390	19.0	.4809	1.468
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				26.7	.6773	2.068
ADIPOSE:										
Kidney	1	.1	N/A	.2713	392	1445	1445	19.7	.4998	.305
	2			.0000	0	0				
Epididymis	1	1	N/A	.2696	441	1636	1636	22.3	.5659	.346
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2085	773	3707	3707	50.6	1.2825	.783
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				30.9	.7827	.478
LIVER:	1	4	10.1212	.4380	12330	28151	27647	377.7	9.5641	2.104
	2			.5300	14580	27509				
	3			.3820	10450	27356				
	4			.3620	9981	27572				
III. GI TRACT TISSUES										
Esophagus		1		.2009	.2009	3056	15202	15202	207.7	5.2588	.023
Stomach	1	1	2.5254	2.5254	140820	55761	55761	761.8	19.2899	1.059
	2			.0000	0	0				
Sm. Intest	1	1	6.7787	6.7787	14680	2166	2166	29.6	.7492	.110
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	4.7349	4.7349	1816	384	384	5.2	.1327	.014
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	3.3682	3.3682	4878	1448	1448	19.8	.5010	.037
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.8869	2.8869	5919	2050	2050	28.0	.7093	.065
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.6443	.6443	2743	4257	4257	58.2	1.4728	.021
	2			.0000	0	0				
Prostate		1	.2638	.2638	1050	3980	3980	54.4	1.3769	.009
V. OTHER TISSUES										
Trachea		1	.1950	.1950	1356	6954	6954	95.0	2.4056	.010
Lungs	1	1	1.1032	1.1032	5220	4732	4732	64.6	1.6369	.039
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0557	.0557	557	10000	10000	136.6	3.4594	.004
Spleen	1	1	.6147	.6147	3275	5328	5328	72.8	1.8431	.025
	2			.0000	0	0				
Kidneys	1	1	2.0999	2.0999	10783	5135	5135	70.2	1.7764	.081
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2864	.2864	420	1466	1466	20.0	.5073	.003
	2			.0000	0	0				
Brain	1	1	1.7886	1.7886	3427	1916	1916	26.2	.6628	.026
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.7839	.7839	2335	2979	2979	40.7	1.0304	.018
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A11. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 0.67 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-121-7

TISSUE ANALYSIS

STUDY ID: CROT-3 Length (hrs): 72 Route: ORAL Dose date: 09-06-83 (MM-DD-YY)

ANIMAL ID: 4188-121-7 ORANGE Rat Strain: F344 MALE Body Wt. (g) 272.0

DOSE Act: .638 mg/kg
.174 mg Cmpd
1.23e7 dpm
Ref: 4188-127 Notebook-page for dose data.
Spec. Act: 73.2 dpm/ng 14C-Cmpd; ref. p. 4188-128

Vehicle: 10% ETOH

RTI Project 310-2227 File Name: CROT-3
Master Protocol 89 edited: 041084-PP
Today's Date: 5/ 8/1984 Template: 0
Compound: Crotonaldehyde

TISSUE		No.of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2680	647	2609	2647	36.2	1.000	.369
	2			.3780	939	2484				
	3			.3358	873	2855				
	4			.2023	534	2640				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1774	1012	5705	5677	77.6	2.145	1.883
	2			.1184	669	5650				
Neck	1	1	N/A	.5826	2981	5117	5117	69.9	1.933	1.697
	2			.0000	0	0				
Abdomen	1	1	N/A	.3428	960	2800	2800	38.3	1.058	.929
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.4610	1620	3514	3514	48.0	1.328	1.166
	2			.0000	0	0				
AVERAGES FOR SKIN								58.4	1.616	1.419
MUSCLE:										
Neck	1	1	N/A	.5527	1078	1950	1950	26.6	.737	2.157
	2			.0000	0	0				
Abdomen	1	1	N/A	.5716	883	1545	1545	21.1	.584	1.708
	2			.0000	0	0				
Hindleg	1	1	N/A	.5135	540	1052	1052	14.4	.397	1.163
	2			.0000	0	0				
AVERAGES FOR MUSCLE								20.7	.573	1.676
ADIPOSE:										
Kidney	1	1	N/A	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
Epididymis	1	1	N/A	.2391	304	1271	1271	17.4	.480	.281
	2			.0000	0	0				
Mesenteric	1	1	N/A	.3837	1289	3359	3359	45.9	1.269	.743
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								21.1	.583	.341
LIVER:	1	4	9.1687	.4790	10776	22497	22589	308.6	8.534	1.684
	2			.4280	9580	22383				
	3			.2770	6321	22819				
	4			.3690	8338	22658				
III. GI TRACT TISSUES										
Esophagus		1	.2294	.2294	2015	8784	8784	120.0	3.319	.016
Stomach	1	1	3.3293	3.3293	84747	25455	25455	347.7	9.617	.689
	2			.0000	0	0				
Sm. Intest	1	1	5.3432	5.3432	10450	1956	1956	26.7	.739	.085
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	4.5434	4.5434	2361	520	520	7.1	.196	.019
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	2.7393	2.7393	3597	1313	1313	17.9	.496	.029
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	3.0635	3.0635	5340	1743	1743	23.8	.659	.043
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.5734	.5734	2202	3840	3840	52.5	1.451	.018
	2			.0000	0	0				
Prostate		1	.3418	.3418	1234	3610	3610	49.3	1.364	.010
V. OTHER TISSUES										
Trachea		1	.1638	.1638	936	5714	5714	78.1	2.159	.008
Lungs	1	1	1.0362	1.0362	4672	4509	4509	61.6	1.703	.038
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0664	.0664	678	10211	10211	139.5	3.858	.006
Spleen	1	1	.5377	.5377	2710	5040	5040	68.9	1.904	.022
	2			.0000	0	0				
Kidneys	1	1	1.94%	1.94%	8927	4579	4579	62.6	1.730	.073
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2791	.2791	369	1322	1322	18.1	.499	.003
	2			.0000	0	0				
Brain	1	1	1.8950	1.8950	3203	1690	1690	23.1	.639	.026
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.8211	.8211	2152	2621	2621	35.8	.990	.017
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A12. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 34 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-77-2

TISSUE ANALYSIS

STUDY ID: CROT-1 Length (hrs): 72 Route: ORAL Dose date: 08-23-83 (MM-DD-YY)

ANIMAL ID: 4188-77-2 ORANGE Rat Strain: F334 MALE Body Wt. (g) 248.0

DOSE Amt: 33.8 mg/kg
8.382 mg Cmpd
4e7 dpm
Ref: 4188-77 Notebook-wage for dose data.
Spec. Act: 6.8 dpm/ng 14C-Cmpd; ref. p. 4188-99

Vehicle: 10% ETOH

RTI Project 310-2227 File Name: Crot-1
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound: crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2942	3262	11088	11082	2308.7	1.000	.433
	2			.2873	3202	11145				
	3			.3089	3419	11068				
	4			.3034	3345	11025				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3333	7740	23243	23243	4842.3	2.097	2.162
	2			.0000	0	0				
Neck	1	1	N/A	.2777	3305	11901	11901	2479.4	1.074	1.107
	2			.0000	0	0				
Abdomen	1	1	N/A	.2225	3193	14351	14351	2989.7	1.295	1.335
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.1501	2819	18781	18781	3912.7	1.695	1.747
	2			.0000	0	0				
AVERAGES FOR SKIN								3556.0	1.540	1.587
MUSCLE:										
Neck	1	1	N/A	.2942	2163	7352	7352	1531.7	.663	2.279
	2			.0000	0	0				
Abdomen	1	1	N/A	.3217	1668	5185	5185	1080.2	.468	1.607
	2			.0000	0	0				
Hindleg	1	1	N/A	.5569	2536	4537	4537	945.3	.409	1.407
	2			.0000	0	0				
AVERAGES FOR MUSCLE								1185.7	.514	1.764
ADIPOSE:										
Kidney	1	1	N/A	.2490	1925	7731	7731	1610.6	.698	.479
	2			.0000	0	0				
Epididymis	1	1	N/A	.2609	1376	5712	5712	1190.0	.515	.354
	2			.0000	0	0				
Mesenteric	1	1	N/A	.3265	5454	16704	16704	3480.1	1.507	1.036
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								2093.6	.907	.623
LIVER:	1	4	8.0164	.4230	10909	25790	26083	5433.9	2.354	.523
	2			.3890	9990	25681				
	3			.3090	8123	26288				
	4			.4280	11373	26572				
III. GI TRACT TISSUES										
Esophagus		1	.2292	.2292	7153	31209	31209	6501.8	2.816	.018
Stomach	1	1	1.4175	1.4175	51520	36346	36346	7572.0	3.280	.129
	2			.0000	0	0				
Sm. Intest	1	1	2.1179	2.1179	54070	25530	25530	5318.8	2.304	.135
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.8022	.8022	11105	13843	13843	2884.0	1.249	.028
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.9042	.9042	14840	16412	16412	3419.2	1.481	.037
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.6290	2.6290	40126	15263	15263	3179.8	1.377	.100
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.4569	.4569	9203	20142	20142	4196.3	1.818	.023
	2			.0000	0	0				
Prostate		1	.4719	.4719	7608	16122	16122	3358.8	1.455	.019
V. OTHER TISSUES										
Trachea		1	.1769	.1769	5653	31391	31391	6539.7	2.833	.014
Lungs	1	1	.8436	.8436	15155	17965	17965	3742.6	1.621	.038
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0295	.0295	1531	51898	51898	10812.1	4.683	.004
Spleen	1	1	.4334	.4334	10147	23413	23413	4877.6	2.113	.025
	2			.0000	0	0				
Kidneys	1	1	1.7872	1.7872	38820	21721	21721	4525.2	1.960	.097
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2672	.2672	1400	5663	5663	1179.9	.511	.004
	2			.0000	0	0				
Brain	1	1	1.4707	1.4707	16036	10904	10904	2271.6	.984	.060
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A13. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 34 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-77-3

TISSUE ANALYSIS

STUDY ID: CROT-1 Length (hrs): 72 Route: ORAL Dose date: 08-23-83 (MM-DD-YY)

ANIMAL ID: 4188-77-3 GREEN Rat Strain: F344 MALE Body Wt. (g) 268.0

DOSE Amt: 36.3 mg/kg
9.728 mg Cmpd
4.7e7 dpm
Ref: 4188-77 Notebook-page for dose data.
Spec. Act: 4.8 dpm/ng 14C-Cmpd. ref. p. 4188-FP

Vehicle: 10% ETOH

RTI Project 310-2227 File Name Crot-1
Master Protocol FP edited: 04108a-FP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3616	4143	12128	12226	2547.1	1.0000	.439
	2			.3569	4338	12087				
	3			.3291	3977	12145				
	4			.3193	4005	12543				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3333	7859	23579	23579	4912.4	1.9286	2.017
	2			.0000	0	0				
Neck	1	1	N/A	.2225	1793	8058	8058	1678.8	.6591	.689
	2			.0000	0	0				
Abdomen	1	1	N/A	.2777	4989	17965	17965	3742.8	1.4695	1.537
	2			.0000	0	0				
Hindmbrs	1	1	N/A	.1501	1424	9487	9487	1976.5	.7760	.811
	2			.0000	0	0				
				AVERAGES FOR SKIN				3077.6	1.2083	1.264
MUSCLE:										
Neck	1	1	N/A	.2962	2203	7408	7408	1540.0	.6125	2.135
	2			.0000	0	0				
Abdomen	1	1	N/A	.5569	2124	3800	3800	791.7	.3108	1.083
	2			.0000	0	0				
Hindleg	1	1	N/A	.3217	1900	5906	5906	1230.4	.4831	1.684
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				1194.1	.4688	1.634
ADIPOSE:										
Kidney	1	1	N/A	.2042	1788	8756	8756	1824.2	.7162	.499
	2			.0000	0	0				
Epididymis	1	1	N/A	.2514	1099	4372	4372	910.7	.3576	.249
	2			.0000	0	0				
Mesenteric	1	1	N/A	.1843	2058	11167	11167	2326.4	.9134	.637
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				1687.1	.6624	.462
LIVER:	1	4	9.0946	.5460	21390	37792	36985	7705.2	3.0251	.716
	2			.4710	17590	37346				
	3			.4790	17760	37077				
	4			.4210	15040	35724				
III. GI TRACT TISSUES										
Esophagus		1	.2242	.2242	8179	36481	36481	7600.2	2.9839	.017
Stomach	1	1	1.7208	1.7208	83570	48565	48565	10117.6	3.9723	.178
	2			.0000	0	0				
Sm. Intest	1	1	2.9557	2.9557	40820	23798	23798	4957.9	1.9465	.129
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	1.0742	1.0742	9068	8442	8442	1758.7	.6905	.019
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.1203	1.1203	20110	17951	17951	3739.7	1.4682	.043
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.7851	2.7851	25570	9181	9181	1912.7	.7509	.054
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.4975	.4975	7131	14334	14334	2986.2	1.1724	.015
	2			.0000	0	0				
Prostate		1	.2286	.2286	3588	15696	15696	3269.9	1.2838	.008
V. OTHER TISSUES										
Trachea		1	.1714	.1714	3034	17701	17701	3687.8	1.4479	.006
Lungs	1	1	.8436	.8436	25720	30488	30488	6351.7	2.4938	.055
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0066	.0066	1045	51972	51972	10827.5	4.2510	.004
Spleen	1	1	.5700	.5700	13250	23246	23246	4842.8	1.9013	.028
	2			.0000	0	0				
Kidneys	1	1	1.7872	1.7872	41600	23277	23277	4849.3	1.9039	.089
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2634	.2634	1400	5752	5752	1198.3	.4705	.003
	2			.0000	0	0				
Brain	1	1	1.4699	1.4699	16350	10989	10989	2289.3	.8988	.039
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.7267	.7267	8232	11314	11314	2357.1	.9254	.017
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A14. Concentration of ^{14}C in Selected Tissues 72 h after Oral Administration of 34 mg/kg [^{14}C]Crotonaldehyde to Rat 4188-77-4

TISSUE ANALYSIS

STUDY ID: CROT-1 Length (hrs): 72 Route: ORAL Dose date: 08-23-83 (MM-DD-YY)

ANIMAL ID: 4188-77-4 YELLOW Rat Strain: F344 MALE Body Wt. (g) 269.0

DOSE Amt: 32.2 mg/kg
8.662 mg Cmpd
4.2e7 dpm
Ref: 4188-77 Notebook-page for dose data.
Spec. Act: 4.8 dpm/ng 14C-Cmpd, ref. p. 4188-99

Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: Crot-1
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No.of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	3	N/A	.0000	0	0	10519	2191.4	1.000	.424
	2			.3405	3958	11624				
	3			.3381	3353	9917				
	4			.3426	3429	10015				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3920	8048	20531	20531	4277.2	1.952	1.972
	2			.0000	0	0				
Neck	1	1	N/A	.2946	3417	11599	11599	2416.4	1.103	1.114
	2			.0000	0	0				
Abdomen	1	1	N/A	.1784	2401	13459	13459	2803.9	1.279	1.293
	2			.0000	0	0				
Hindetrs	1	1	N/A	.4079	4860	11915	11915	2482.2	1.133	1.145
	2			.0000	0	0				
AVERAGES FOR SKIN								2994.9	1.367	1.381
MUSCLE:										
Neck	1	1	N/A	.2125	1460	6871	6871	1431.4	.653	2.200
	2			.0000	0	0				
Abdomen	1	1	N/A	.6852	2851	4161	4161	866.8	.396	1.332
	2			.0000	0	0				
Hindleg	1	1	N/A	.3493	1306	3739	3739	778.9	.355	1.197
	2			.0000	0	0				
AVERAGES FOR MUSCLE								1025.7	.468	1.577
ADIPOSE:										
Kidney	1	1	N/A	.2808	1298	4623	4623	963.0	.439	.296
	2			.0000	0	0				
Epididymis	1	1	N/A	.2868	1761	6070	6070	1264.7	.577	.389
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2805	2930	10446	10446	2176.2	.993	.669
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								1468.0	.670	.451
LIVER:	1	4	9.1930	.4660	15040	33722	34686	7226.2	3.298	.759
	2			.3360	11610	34554				
	3			.5060	17940	35455				
	4			.3990	13620	35013				
III. GI TRACT TISSUES										
Esophagus		1	.2077	.2077	6972	33568	33568	6993.3	3.191	.017
Stomach	1	1	1.6362	1.6362	78250	47824	47824	9963.4	4.547	.186
	2			.0000	0	0				
Sm. Intest	1	1	2.6925	2.6925	48670	18076	18076	3765.9	1.718	.116
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.8265	.8265	7591	9185	9185	1913.4	.873	.018
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.9996	.9996	17730	17737	17737	3695.2	1.686	.042
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.7227	2.7227	22920	8418	8418	1753.8	.800	.056
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.4502	.4502	6229	13836	13836	2882.5	1.315	.015
	2			.0000	0	0				
Prostate		1	.2760	.2760	4150	15036	15036	3132.5	1.429	.010
V. OTHER TISSUES										
Trachea		1	.2070	.2070	3696	17855	17855	3719.8	1.697	.009
Lungs	1	1	1.1435	1.1435	16870	14753	14753	3073.5	1.403	.040
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0429	.0429	2186	50956	50956	10615.8	4.844	.005
Spleen	1	1	.5258	.5258	11013	20945	20945	4363.6	1.991	.026
	2			.0000	0	0				
Kidneys	1	1	1.7595	1.7595	40630	23092	23092	4810.8	2.195	.097
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
Brain	1	1	1.7580	1.7580	17910	10188	10188	2122.4	.969	.043
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	2	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A15. Concentration of ^{14}C in Selected Tissues 0.25 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-87-1

TISSUE ANALYSIS

STUDY ID: CROT-10 Length (hrs): .25 Route: IV Dose date: 12-9-83 (MM-DD-YY)

ANIMAL ID: 4275-87-1 YELLOW Rat Strain: F334 MALE Body Wt. (g) 328.0

DOSE Amt: 2.68 mg/kg
.945 mg Cmpd
1.04e7 dpm
Ref: 4275-90 Notebook-page for dose data.
Spec. Act: 11 dpm/mg 14C-Cmpd, ref. p. 4275-90

Vehicle: 10% ETOH

RTI Project 311-2227 File Name: CROT-10
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.1951	24600	126089	126798	11527.1	1.000	25.194
	2			.2172	27600	127072				
	3			.2163	27400	126676				
	4			.1751	22300	127356				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.1777	1970	11086	11086	1007.8	.087	5.245
	2			.0000	0	0				
Neck	1	1	N/A	.0000	0	0	12354	1123.1	.097	5.844
	2			.2744	3390	12354				
Abdomen	1	2	N/A	.1493	2310	15472	14596	1326.9	.115	6.905
	2			.1086	1490	13720				
Hindlmbs	1	2	N/A	.1234	1050	8509	10477	952.5	.083	4.957
	2			.1382	1720	12446				
				AVERAGES FOR SKIN				1102.6	.096	5.738
MUSCLE:										
Neck	1	2	N/A	.1582	2170	13717	12923	1174.8	.102	20.379
	2			.2127	2580	12130				
Abdomen	1	2	N/A	.2907	2820	9701	9492	862.9	.075	14.968
	2			.4104	3810	9284				
Hindleg	1	2	N/A	.2063	1990	9646	10221	929.2	.081	16.117
	2			.2075	2260	10795				
				AVERAGES FOR MUSCLE				989.0	.086	17.155
ADIPOSE:										
Kidney	1	2	N/A	.2017	432	2142	1960	178.2	.015	.618
	2			.2767	492	1778				
Epididymis	1	2	N/A	.3154	651	2064	1951	177.3	.015	.615
	2			.1611	296	1837				
Mesenteric	1	2	N/A	.2104	1220	5798	4698	427.1	.037	1.482
	2			.1345	486	3599				
				AVERAGES FOR ADIPOSE				260.9	.023	.905
LIVER:	1	4	11.2965	.3585	17130	47782	47437	4312.5	.374	5.153
	2			.4004	19200	47952				
	3			.3108	14680	47233				
	4			.3693	17230	46683				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A16. Concentration of ^{14}C in Selected Tissues 0.25 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-87-2

TISSUE ANALYSIS

STUDY ID: CROT-10 Length (hrs): .25 Route: IV Dose date: 12-9-83 (MM-DD-YY)

ANIMAL ID: 4275-87-2 RED Rat Strain: F334 MALE Body Wt. (g) 325.0

DOSE Amt: 2.86 mg/kg
.923 mg Cmpd
1.02e7 dpm
Ref: 4275-90 Notebook-page for dose data.
Spec. Act: 11 dpm/ng 14C-Cmpd, ref. p. 4275-90
Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-10
Master Protocol 89 edited: DA1084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	3	N/A	.0000	0	0	125637	11421.5	1.0000	25.220
	2			.1443	18200	126126				
	3			.1608	20000	124378				
	4			.1867	23600	126406				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.2535	3340	13176	12675	1152.3	.1009	6.058
	2			.2193	2670	12175				
Neck	1	2	N/A	.1002	1330	13273	12920	1174.5	.1028	6.175
	2			.0752	965	12566				
Abdomen	1	2	N/A	.1062	1800	16949	16117	1465.2	.1283	7.703
	2			.1001	1530	15285				
Hindqtrs	1	2	N/A	.0682	629	9223	8851	777.4	.0681	4.087
	2			.0547	431	7879				
				AVERAGES FOR SKIN				1142.3	.1000	6.006
MUSCLE:										
Neck	1	1	N/A	.2648	3530	13331	13331	1211.9	.1061	21.238
	2			.0000	0	0				
Abdomen	1	2	N/A	.0000	0	0	0	.0	.0000	.000
	2			.0000	0	0				
Hindleg	1	1	N/A	.0000	0	0	9704	882.2	.0772	15.460
	2			.6389	6200	9704				
				AVERAGES FOR MUSCLE				1047.0	.0916	18.349
ADIPOSE:										
Kidney	1	2	N/A	.2622	750	3097	3901	354.7	.0311	1.243
	2			.1190	560	4706				
Epididymis	1	2	N/A	.2785	825	2962	2773	252.1	.0221	.884
	2			.1498	387	2583				
Mesenteric	1	2	N/A	.3231	2970	9192	9470	860.9	.0754	3.017
	2			.3129	3050	9748				
				AVERAGES FOR ADIPOSE				489.2	.0428	1.715
LIVER:	1	4	11.9290	.3938	17430	44261	44409	4037.2	.3535	5.194
	2			.2990	13430	44916				
	3			.2321	10230	44076				
	4			.2519	11180	44383				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A17. Concentration of ^{14}C in Selected Tissues 0.25 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-87-3

TISSUE ANALYSIS

STUDY ID: CROT-10 Length (hrs): .25 Route: IV Dose date: 12-9-83 (MM-DD-YY)

ANIMAL ID: 4275-87-3 PURPLE Rat Strain: F334 MALE Body Wt. (g) 330.0

DOSE Act: 2.88 mg/kg
.950 mg Cmpd
1.05e7 dpm
Ref: 4275-90 Notebook-page for dose data.
Spec. Act: 11 dpm/ng 14C-Cmpd, ref. p. 4275-90

Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-10
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: 0
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	3	N/A	.0000	0	0	124441	11312.8	1.000	26.639
	2			.1726	21200	122827				
	3			.1737	22000	126655				
	4			.1938	24000	123839				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.1575	1950	12381	12381	1125.5	.099	5.837
	2			.0000	0	0				
Neck	1	2	N/A	.0978	1380	14110	13619	1229.0	.109	6.373
	2			.1315	1700	12928				
Abdomen	1	2	N/A	.3403	5770	16956	16434	1496.0	.132	7.767
	2			.2187	3480	15912				
Hindquts	1	2	N/A	.2351	2400	10208	11571	1051.9	.093	5.455
	2			.3495	4520	12933				
				AVERAGES FOR SKIN				1225.1	.108	6.353
MUSCLE										
Neck	1	2	N/A	.2383	2750	11540	13150	1195.4	.106	20.664
	2			.2805	4140	14759				
Abdomen	1	2	N/A	.1884	2250	11943	11946	1086.0	.096	18.772
	2			.3632	4340	11949				
Hindleg	1	2	N/A	.4251	4610	10845	10095	917.7	.081	15.864
	2			.3392	3170	9346				
				AVERAGES FOR MUSCLE				1066.4	.094	18.433
ADIPOSE:										
Kidney	1	2	N/A	.2144	548	2556	2307	209.7	.019	.725
	2			.4616	950	2058				
Epididymis	1	2	N/A	.2319	660	2846	3966	360.5	.032	1.246
	2			.2733	1390	5086				
Mesenteric	1	1	N/A	.1089	1090	10009	10009	909.9	.080	3.146
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				493.4	.044	1.706
LIVER:	1	4	10.9181	.4338	19350	44606	44959	4087.2	.361	4.675
	2			.2911	12990	44624				
	3			.2907	13130	45167				
	4			.2766	12560	45441				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight, skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A18. Concentration of ^{14}C in Selected Tissues 0.75 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-81-1

TISSUE ANALYSIS

STUDY ID: CROT-9 Length (hrs): .75 Route: IV Dose date: 12-7-83 (MM-DD-YY)

ANIMAL ID: 4275-81-1 WHITE Rat Strain: F334 MALE Body Wt. (g) 334.0

DOSE Act: 2.91 mg/kg
.972 mg Cmpd
1.08e7 dpm
Ref: 4275-80 Notebook-wage for dose data.
Spec. Act: 11.1 dpm/ng ^{14}C-Cmpd; ref. p. 4275-79

Vehicle: 10% ETOH

RTI Project 310-2227 File Name: CROT-9
Master Protocol 89 edited: 041084-PP
Today's Date: 0 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.1696	10000	59032	58471	5267.7	1.000	11.392
	2			.2406	14200	59019				
	3			.1746	10100	57847				
	4			.1897	11000	57986				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1925	2230	11584	11463	1032.7	.196	5.318
	2			.1490	1690	11342				
Neck	1	2	N/A	.1346	1650	12259	13120	1182.0	.224	6.086
	2			.1552	2170	13982				
Abdomen	1	2	N/A	.1236	1580	12783	12090	1089.2	.207	5.608
	2			.1325	1510	11396				
Hindlimb	1	2	N/A	.1429	1570	10987	10565	951.8	.181	4.901
	2			.2238	2270	10143				
				AVERAGES FOR SKIN				1063.9	.202	5.478
MUSCLE:										
Neck	1	2	N/A	.2210	2130	9638	9661	870.4	.165	14.939
	2			.2313	2240	9684				
Abdomen	1	2	N/A	.2612	2220	8499	8440	760.4	.144	13.051
	2			.2634	2040	8381				
Hindleg	1	2	N/A	.1798	1650	9177	8879	799.9	.152	13.729
	2			.2572	2207	8581				
				AVERAGES FOR MUSCLE				810.2	.154	13.907
ADIPOSE:										
Kidney	1	2	N/A	.3152	189	600	1191	107.3	.020	.368
	2			.3104	553	1782				
Epididymis	1	2	N/A	.3392	499	1471	1903	171.5	.033	.589
	2			.2351	549	2335				
Mesenteric	1	2	N/A	.0907	323	3561	3352	302.0	.057	1.037
	2			.1015	319	3143				
				AVERAGES FOR ADIPOSE				193.6	.037	.664
LIVER:	1	4	10.8742	.2960	11960	40680	40359	3635.9	.690	4.064
	2			.2157	8770	40658				
	3			.4410	17750	40249				
	4			.4693	18700	39847				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A19. Concentration of ^{14}C in Selected Tissues 0.75 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-81-3

TISSUE ANALYSIS

STUDY ID: CROT-9 Length (hrs): .75 Route: IV Dose date: 12-7-83 (MM-DD-YY)

ANIMAL ID: 4275-81-3 PINK Rat Strain: F334 MALE Body Wt. (g) 335.0

DOSE Amt: 2.74 mg/kg
.918 mg Cmpd
1.03e7 dpm
Ref: 4275-80 Notebook-page for dose data.
Spec. Act: 11.1 dpm/ng 14C-Cmpd, ref. p. 4275-79

Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-9
Master Protocol 89 edited: 061084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	2	N/A	.2818	20400	72392	72232	6507.4	1.0000	14.801
	2			.2886	20800	72072				
	3			.0000	0	0				
	4			.0000	0	0				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1346	1500	11144	11362	1023.6	.1573	5.543
	2			.2228	2580	11580				
Neck	1	2	N/A	.1761	2150	12349	11638	1048.5	.1611	5.678
	2			.1565	1710	10927				
Abdomen	1	2	N/A	.2092	2790	13337	14626	1317.6	.2025	7.135
	2			.1640	2610	15915				
Hindotrs	1	2	N/A	.1695	1620	9498	10999	990.9	.1523	5.366
	2			.0816	1020	12500				
				AVERAGES FOR SKIN				1095.1	.1683	5.931
MUSCLE:										
Neck	1	2	N/A	.4506	4510	10009	9865	888.7	.1366	16.042
	2			.3899	3790	9720				
Abdomen	1	2	N/A	.2834	2580	9104	8821	794.7	.1221	14.345
	2			.5036	4300	8539				
Hindleg	1	1	N/A	.2307	1890	8192	8192	738.1	.1134	13.323
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				807.2	.1240	14.570
ADIPOSE:										
Kidney	1	2	N/A	.1689	275	1847	1765	159.0	.0244	.574
	2			.1682	283	1683				
Epididymis	1	2	N/A	.2037	1340	6578	5676	511.3	.0786	1.846
	2			.1232	588	4773				
Mesenteric	1	2	N/A	.1214	410	3377	3437	309.6	.0476	1.118
	2			.1124	393	3496				
				AVERAGES FOR ADIPOSE				326.6	.0502	1.179
LIVER:	1	4	9.5485	.3049	11572	37953	37866	3411.3	.5242	3.510
	2			.2920	10838	37116				
	3			.2061	7838	38030				
	4			.2237	8582	38364				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A20. Concentration of ^{14}C in Selected Tissues 0.75 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-81-4

TISSUE ANALYSIS

STUDY ID: CROT-9 Length (hrs): .75 Route: IV Dose date: 12-7-83 (MM-DD-YY)

ANIMAL ID: 4275-81-4 GREEN Rat Strain: F334 MALE Body Wt. (g) 309.0

DOSE Amt: 2.89 mg/kg
.893 mg Cmpd
9.93e6 dpm
Ref: 4275-80 Notebook-page for dose data.
Spec. Act: 11.1 dpm/ng 14C-Cmpd, ref. p. 4275-79
Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-9
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: 0
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2252	14100	62611	63140	5688.3	1.000	12.378
	2			.1554	9850	63385				
	3			.1540	9810	63701				
	4			.1551	9750	62863				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1233	1360	10949	10807	973.6	.171	5.044
	2			.1369	1460	10665				
Neck	1	2	N/A	.1037	1140	10993	10826	975.1	.171	5.052
	2			.1436	1530	10655				
Abdomen	1	2	N/A	.1193	1830	15339	15226	1371.7	.241	7.107
	2			.1780	2690	15112				
Hindqtrs	1	2	N/A	.2433	2560	10522	10193	918.3	.161	4.758
	2			.2210	2180	9864				
				AVERAGES FOR SKIN				1059.7	.186	5.490
MUSCLE:										
Neck	1	2	N/A	.2536	2090	8241	8409	757.6	.133	13.084
	2			.2833	2430	8577				
Abdomen	1	2	N/A	.4079	3160	7747	7590	683.8	.120	11.809
	2			.2220	1650	7432				
Hindleg	1	2	N/A	.2026	1500	7404	7923	713.8	.125	12.328
	2			.2203	1860	8443				
				AVERAGES FOR MUSCLE				718.4	.126	12.407
ADIPOSE:										
Kidney	1	2	N/A	.2060	314	1524	1566	140.9	.025	.487
	2			.2370	380	1603				
Epididymis	1	2	N/A	.1905	411	2157	1893	170.6	.030	.589
	2			.1590	259	1629				
Mesenteric	1	2	N/A	.1294	733	5665	6329	570.2	.100	1.969
	2			.1570	1098	6994				
				AVERAGES FOR ADIPOSE				293.9	.052	1.015
LIVER:	1	4	10.2934	.2850	10753	37730	37839	3408.9	.599	3.922
	2			.2374	9061	38168				
	3			.2534	9589	37841				
	4			.1847	6948	37618				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A21. Concentration of ^{14}C in Selected Tissues 2 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-57-2

TISSUE ANALYSIS

STUDY ID: CROT-8 Length (hrs): 2 Route: IV Dose date: 11-11-83 (MM-DD-YY)

ANIMAL ID: 4275-57-2 ORANGE Rat Strain: F334 MALE Body Wt. (g) 317.0

DOSE Amt: 2.91 mg/kg
.922 mg Cpd
1.33e7 dpm
Ref: 4275-59 Notebook page for dose data.
Spec. Act: 14.5 dpm/ng 14C-Cpd; ref. p. 4275-56
Vehicle: 10% ETOH

RTI Project: 311-2227 File Name: CROT-8
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3838	12610	32856	33169	2287.5	1.000	4.981
	2			.2473	8299	33558				
	3			.2174	7207	33151				
	4			.2521	8347	33110				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.212A	1550	7298	7298	503.3	.220	2.609
	2			.0000	0	0				
Neck	1	1	N/A	.1858	1140	6136	6136	423.1	.185	2.196
	2			.0000	0	0				
Abdomen	1	1	N/A	.2709	3216	11872	11872	818.7	.358	4.264
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.2287	2098	9174	9174	632.7	.277	3.280
	2			.0000	0	0				
				AVERAGES FOR SKIN				594.5	.260	3.082
MUSCLE:										
Neck	1	1	N/A	.4760	2660	5588	5588	385.4	.168	6.660
	2			.0000	0	0				
Abdomen	1	1	N/A	.7897	3790	4799	4799	331.0	.145	5.719
	2			.0000	0	0				
Hindleg	1	1	N/A	.4963	2290	4614	4614	318.2	.139	5.499
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				344.9	.151	5.959
ADIPOSE:										
Kidney	1	1	N/A	.4877	904	1854	1854	127.8	.056	.442
	2			.0000	0	0				
Epididymis	1	1	N/A	.4544	875	1926	1926	132.8	.058	.459
	2			.0000	0	0				
Mesenteric	1	1	N/A	.3755	1810	4820	4820	332.4	.145	1.149
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				197.7	.086	.683
LIVER:	1	4	13.2270	.2438	7474	30656	30881	2129.7	.931	3.071
	2			.2529	7829	30957				
	3			.2555	7869	30798				
	4			.1996	6204	31113				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A22. Concentration of ^{14}C in Selected Tissues 2 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-57-3

TISSUE ANALYSIS

STUDY ID: CROT-8 Length (hrs): 2 Route: IV Dose date: 11-11-83 (MM-DD-YY)

ANIMAL ID: 4275-57-3 GREEN Rat Strain: F344 MALE Body Wt. (g) 307.0

DOSE Amt: 2.99 mg/kg
.918 mg Cmpd
1.33e7 dpm
Ref: 4275-59 Notebook-page for dose data.
Spec. Act: 14.5 dpm/ng 14C-Cmpd, ref. p. 4275-56
Vehicle: 10% ETOH

RTI Project 3110-2227 File Name: CROT-8
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2108	7433	35261	35291	2433.8	1.0000	5.132
	2			.2512	8970	35709				
	3			.3351	11683	34864				
	4			.3487	12319	35328				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.2534	1950	7695	7695	530.7	.2181	2.664
	2			.0000	0	0				
Neck	1	1	N/A	.1852	1580	8531	8531	588.4	.2417	2.954
	2			.0000	0	0				
Abdomen	1	1	N/A	.1922	1440	7492	7492	516.7	.2123	2.594
	2			.0000	0	0				
Hindlmbs	1	1	N/A	.2962	2930	9892	9892	682.2	.2803	3.425
	2			.0000	0	0				
				AVERAGES FOR SKIN				579.5	.2381	2.909
MUSCLE:										
Neck	1	1	N/A	.0000	0	0	0	.0	.0000	.000
	2			.0000	0	0				
Abdomen	1	1	N/A	.5384	3070	5702	5702	393.2	.1616	6.581
	2			.0000	0	0				
Hindleg	1	1	N/A	.3597	1944	5405	5405	372.7	.1531	6.238
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				383.0	.1574	6.410
ADIPOSE:										
Kidney	1	1	N/A	.0000	0	0	0	.0	.0000	.000
	2			.0000	0	0				
Epididymis	1	1	N/A	.2548	424	1664	1664	114.8	.0472	.384
	2			.0000	0	0				
Mesenteric	1	1	N/A	.0890	402	4517	4517	311.5	.1280	1.043
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				213.2	.0876	.714
LIVER:	1	4	12.3648	.2460	8441	34313	34734	2395.4	.9842	3.229
	2			.2256	7876	34911				
	3			.2890	10035	34723				
	4			.2380	8327	34987				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A23. Concentration of ^{14}C in Selected Tissues 2 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-57-4

TISSUE ANALYSIS

STUDY ID: CROT-8 Length (hrs): 2 Route: IV Dose date: 11-11-83 (MM-DD-YY)

ANIMAL ID: 4275-57-4 PINK Rat Strain: F334 MALE Body Wt. (g) 300.0

DOSE Amt: 2.88 mg/kg
.864 mg Cmpd
1.25e7 dpm
Ref: 4275-59 Notebook-page for dose data.
Spec. Act: 14.5 dpm/ng 14C-Cmpd, ref. p. 4275-56
Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-8
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: 0
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3862	13230	34257	34447	2375.6	1.000	5.208
	2			.4491	15530	34580				
	3			.3011	10490	34839				
	4			.3562	12150	34110				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.2581	1920	7439	7439	513.0	.216	2.678
	2			.0000	0	0				
Neck	1	1	N/A	.1826	1150	6298	6298	434.3	.183	2.267
	2			.0000	0	0				
Abdomen	1	1	N/A	.1555	1936	12444	12444	858.2	.361	4.480
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.2028	2240	11045	11045	761.7	.321	3.976
	2			.0000	0	0				
				AVERAGES FOR SKIN				641.8	.270	3.350
MUSCLE:										
Neck	1	1	N/A	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
Abdomen	1	1	N/A	.6469	3970	6137	6137	423.2	.178	7.364
	2			.0000	0	0				
Hindleg	1	1	N/A	.3316	1830	5519	5519	380.6	.160	6.622
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				401.9	.169	6.993
ADIPOSE:										
Kidney	1	1	N/A	.4451	450	1011	1011	69.7	.029	.243
	2			.0000	0	0				
Epididymis	1	1	N/A	.2938	339	1154	1154	79.6	.033	.277
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2251	647	2874	2874	198.2	.083	.690
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				115.8	.049	.403
LIVER:	1	4	10.1422	.2767	7342	26534	26385	1819.7	.766	2.141
	2			.2141	5642	26352				
	3			.3510	9180	26154				
	4			.2466	6535	26500				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lungs	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Adrenals		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A24. Concentration of ^{14}C in Selected Tissues 6 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-178-1

TISSUE ANALYSIS

STUDY ID: CROT-6 Length (hrs): 6 Route: IV Dose date: 10-06-83 (MM-DD-YY)

ANIMAL ID: 4188-178-1 BLUE Rat Strain: F334 MALE Body Wt. (g) 219.0

DOSE Act: 2.62 mg/kg
.574 mg Cmpd
1.41e7 dpm
Ref: 4188-175 Notebook-page for dose data.
Spec. Act: 26.7 dpm/ng 14C-Cmpd; ref. p. 4188-177

Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: CROT-6
Master Protocol 8P edited: 041084-PP
Today's Date: 9/ 8/1984
Compound: crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3090	7235	23414	23347	965.2	1.000	2.285
	2			.5390	12481	23156				
	3			.3126	7345	23496				
	4			.2830	6600	23322				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1163	1302	11195	9985	404.3	.428	2.326
	2			.1715	1505	8776				
Neck	1	1	N/A	.1405	791	5630	5630	227.9	.241	1.312
	2			.0000	0	0				
Abdomen	1	1	N/A	.1806	1885	10437	10437	422.6	.447	2.432
	2			.0000	0	0				
Hindqtrs	1	2	N/A	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
AVERAGES FOR SKIN								351.6	.372	2.023
MUSCLE:										
Neck	1	1	N/A	.2254	969	4299	4299	174.0	.184	3.339
	2			.0000	0	0				
Abdomen	1	1	N/A	.3649	2139	5862	5862	237.3	.251	4.552
	2			.0000	0	0				
Hindleg	1	1	N/A	.4548	1513	3327	3327	134.7	.142	2.584
	2			.0000	0	0				
AVERAGES FOR MUSCLE								182.0	.193	3.491
ADIPOSE:										
Kidney	1	1	N/A	.1486	444	2988	2988	121.0	.128	.464
	2			.0000	0	0				
Epididymis	1	1	N/A	.1560	480	3077	3077	124.6	.132	.478
	2			.0000	0	0				
Mesenteric	1	1	N/A	.1814	1525	8407	8407	340.4	.360	1.306
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								195.3	.207	.749
LIVER:	1	3	7.8277	.3328	6816	20481	20501	830.0	.878	1.138
	2			.3104	6328	20387				
	3			.3958	8168	20637				
	4			.0000	0	0				
III. GI TRACT TISSUES										
Esophagus		1	.2180	.2180	4871	22344	22344	904.6	.957	.035
Stomach	1	1	1.0479	1.0479	17368	16574	16574	671.0	.710	.123
	2			.0000	0	0				
Sm. Intest	1	1	2.1038	2.1038	74330	35331	35331	1430.4	1.513	.527
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.6861	.6861	8577	12501	12501	506.1	.535	.061
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.9956	.9956	23722	23827	23827	964.6	1.021	.168
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.2100	2.2100	16813	7608	7608	308.0	.326	.119
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.7230	.7230	4820	6667	6667	269.9	.286	.034
	2			.0000	0	0				
Prostate		1	.2056	.2056	4563	22194	22194	898.5	.951	.032
V. OTHER TISSUES										
Trachea		1	.1230	.1230	4352	35382	35382	1432.5	1.515	.031
Lungs	1	1	.6626	.6626	27623	41689	41689	1687.8	1.786	.196
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0395	.0395	763	19318	19318	802.4	.849	.005
Spleen	1	1	.3490	.3490	8192	23473	23473	950.3	1.005	.058
	2			.0000	0	0				
Kidneys	1	1	1.7172	1.7172	33389	19444	19444	787.2	.833	.237
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2676	.2676	1566	5852	5852	236.9	.251	.011
	2			.0000	0	0				
Brain	1	1	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.6727	.6727	10066	14964	14964	605.8	.641	.071
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A25. Concentration of ^{14}C in Selected Tissues 6 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-178-2

TISSUE ANALYSIS

STUDY ID: CROT-6 Length (hrs): 6 Route: IV Dose date: 10-06-83 (MM-DD-YY)

ANIMAL ID: 4188-178-2 GREEN Rat Strain: F344 MALE Body Wt. (g) 277.0

DOSE Amt: 2.57 mg/kg .712 mg Cmpd 1.76e7 dpm Vehicle: 10% ETOH

Ref: 4188-175 Notebook-page for dose data. Spec. Act: 24.7 dpm/ng 14C-Cmpd, ref. p. 4188-177

RTI Project 310-2227 File Name: CROT-6 Master Protocol 69 edited: 04108A-PP Today's Date: 9/ 8/1984 Compound:

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	mg-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3179	8153	25646	25708	1040.8	1.0000	2.569
	2			.3109	8050	25893				
	3			.3069	7978	25995				
	4			.2872	7265	25296				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1239	1217	9822	9540	386.2	.3711	2.252
	2			.2343	2169	9257				
Neck	1	1	N/A	.2911	2270	7798	7798	315.7	.3033	1.841
	2			.0000	0	0				
Abdomen	1	1	N/A	.2293	2229	9721	9721	393.6	.3781	2.295
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.3002	3002	10000	10000	404.9	.3890	2.361
	2			.0000	0	0				
AVERAGES FOR SKIN								375.1	.3604	2.187
MUSCLE:										
Neck	1	1	N/A	.2688	1491	5547	5547	224.6	.2158	4.365
	2			.0000	0	0				
Abdomen	1	1	N/A	.5621	2904	5166	5166	209.2	.2010	4.066
	2			.0000	0	0				
Hindleg	1	1	N/A	.2699	1021	3783	3783	153.2	.1472	2.977
	2			.0000	0	0				
AVERAGES FOR MUSCLE								195.6	.1880	3.802
ADIPOSE:										
Kidney	1	1	N/A	.2616	428	1636	1636	66.2	.0636	.257
	2			.0000	0	0				
Epididymis	1	1	N/A	.2286	677	2962	2962	119.9	.1152	.466
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2190	1230	5616	5616	227.4	.2185	.884
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								137.8	.1324	.536
LIVER:	1	3	9.5422	.3460	7536	21780	21665	877.1	.8428	1.175
	2			.3860	8328	21575				
	3			.3195	6914	21640				
	4			.0000	0	0				
III. GI TRACT TISSUES										
Esophagus		1	.2321	.2321	3683	15868	15868	642.4	.6173	.021
Stomach	1	1	1.1502	1.1502	20296	17646	17646	714.4	.6864	.115
	2			.0000	0	0				
Sm. Intest	1	1	3.2051	3.2051	104170	32501	32501	1315.8	1.2643	.592
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.6466	.6466	14588	22561	22561	913.4	.8776	.083
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.3898	1.3898	37625	27072	27072	1096.0	1.0531	.214
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.5891	2.5891	21996	8496	8496	344.0	.3305	.125
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.9614	.9614	2570	2730	2730	110.5	.1062	.015
	2			.0000	0	0				
Prostate		1	.0000	.0000	0	0	0	.0	.0000	.000
V. OTHER TISSUES										
Trachea		1	.1434	.1434	4189	29212	29212	1182.7	1.1363	.026
Lungs	1	1	1.8967	1.8967	53660	28239	28239	1143.3	1.0985	.304
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0724	.0724	1438	19862	19862	804.1	.7726	.008
Spleen	1	1	.5974	.5974	14399	24103	24103	975.8	.9376	.082
	2			.0000	0	0				
Kidneys	1	1	2.1805	2.1805	50809	23302	23302	943.4	.9064	.289
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2907	.2907	1950	6708	6708	271.6	.2609	.011
	2			.0000	0	0				
Brain	1	1	1.6172	1.6172	26760	16547	16547	669.9	.6437	.152
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.8387	.8387	11621	13856	13856	561.0	.5390	.066
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A26. Concentration of ^{14}C in Selected Tissues 6 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-178-3

TISSUE ANALYSIS

STUDY ID: CROT-6 Length (hrs): 6 Route: IV Dose date: 10-06-83 (MM-DD-YY)

ANIMAL ID: 4188-178-3-PINK Rat Strain: F334 MALE Body Wt. (g) 250.0

DOSE Amt: 2.6 mg/kg
.650 mg Cmpd
1.4e7 dpm
Vehicle: 10% ETOH
Ref: 4188-175 Notebook page for dose data.
Spec. Act: 24.7 dpm/ng 14C-Cmpd, ref. p. 4188-177

RTI Project 3110-2227 File Name: CROT-6
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No.of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2263	4871	21525	21362	864.9	1.000	2.103
	2			.3186	6742	21161				
	3			.3589	7403	21184				
	4			.2845	6139	21578				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1318	1282	9727	8871	359.2	.415	2.079
	2			.1532	1228	8016				
Neck	1	1	N/A	.1753	1870	10667	10667	431.9	.499	2.500
	2			.0000	0	0				
Abdomen	1	1	N/A	.1063	758	7131	7131	288.7	.334	1.671
	2			.0000	0	0				
Hindquts	1	1	N/A	.3427	3402	9927	9927	401.9	.465	2.327
	2			.0000	0	0				
				AVERAGES FOR SKIN				370.4	.428	2.144
MUSCLE:										
Neck	1	1	N/A	.2658	1881	7077	7077	286.5	.331	5.529
	2			.0000	0	0				
Abdomen	1	1	N/A	.4226	2543	6018	6018	243.6	.282	4.701
	2			.0000	0	0				
Hindleg	1	1	N/A	.3433	1528	4451	4451	180.2	.208	3.477
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				236.8	.274	4.569
ADIPOSE:										
Kidney	1	1	N/A	.1897	450	2372	2372	96.0	.111	.371
	2			.0000	0	0				
Epididymis	1	1	N/A	.2825	370	1310	1310	53.0	.061	.205
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2277	1268	5569	5569	225.5	.261	.870
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				124.8	.144	.482
LIVER:	1	3	8.6669	.4427	12130	27400	27284	1104.6	1.277	1.478
	2			.2998	8146	27171				
	3			.3828	10443	27281				
	4			.0000	0	0				
III. GI TRACT TISSUES										
Esophagus		1	.2421	.2421	4144	17117	17117	693.0	.801	.026
Stomach	1	1	1.1336	1.1336	16917	14923	14923	604.2	.699	.106
	2			.0000	0	0				
Sm. Intest	1	1	2.9444	2.9444	70762	24033	24033	973.0	1.125	.642
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.4646	.4646	10921	16432	16432	665.3	.769	.068
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.2555	1.2555	28681	22844	22844	924.9	1.069	.179
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.5264	2.5264	16114	6378	6378	258.2	.299	.101
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.6643	.6643	7723	11626	11626	470.7	.544	.068
	2			.0000	0	0				
Prostate		1	.2201	.2201	3030	13766	13766	557.3	.644	.019
V. OTHER TISSUES										
Trachea		1	.1671	.1671	3945	23609	23609	955.8	1.105	.025
Lungs	1	1	1.0139	1.0139	35226	34743	34743	1406.6	1.626	.220
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0542	.0542	979	18063	18063	731.3	.846	.006
Spleen	1	1	.5565	.5565	12437	22349	22349	904.8	1.046	.078
	2			.0000	0	0				
Kidneys	1	1	1.7421	1.7421	36258	20813	20813	842.6	.974	.227
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.3086	.3086	1772	5742	5742	232.5	.269	.011
	2			.0000	0	0				
Brain	1	1	1.2704	1.2704	18588	14632	14632	592.4	.685	.116
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.8084	.8084	10719	13260	13260	536.8	.621	.067
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A27. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-151-1

TISSUE ANALYSIS

STUDY ID: CROT-4 Length (hrs): 24 Route: IV Dose date: 09-21-89 (MM-DD-YY)

ANIMAL ID: 4188-151-1 BLUE Rat Strain: F344 MALE Body Wt. (g) 236.0

DOSE Amt: 2.7% eq/kg
.647 eq Cmpd
1.9e7 dpm
Ref: 4188-153 Notebook page for dose data.
Spec. Act: 30.4 dpm/ng 14C-Cmpd, ref. p. 4251-89
Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: Crot-4
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1986
Compound: crotaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3105	4065	13092	13290	437.2	1.000	1.008
	2			.2355	3097	13151				
	3			.2112	2873	13603				
	4			.1759	2342	13314				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3318	4281	12902	12902	424.4	.971	2.330
	2			.0000	0	0				
Neck	1	1	N/A	.2238	2926	13065	13065	429.8	.983	2.360
	2			.0000	0	0				
Abdomen	1	1	N/A	.1183	1872	15826	15826	520.5	1.191	2.858
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.2184	3218	14734	14734	484.7	1.109	2.661
	2			.0000	0	0				
				AVERAGES FOR SKIN				464.9	1.063	2.552
MUSCLE:										
Neck	1	1	N/A	.3476	1787	5141	5141	169.1	.387	3.095
	2			.0000	0	0				
Abdomen	1	1	N/A	.4584	2206	4812	4812	158.3	.362	2.897
	2			.0000	0	0				
Hindleg	1	1	N/A	.4985	2212	4437	4437	146.0	.334	2.671
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				157.8	.361	2.888
ADIPOSE:										
Kidney	1	1	N/A	.1934	760	3930	3930	129.3	.296	.473
	2			.0000	0	0				
Epididymis	1	1	N/A	.2899	1001	3465	3465	114.0	.261	.417
	2			.0000	0	0				
Mesenteric	1	1	N/A	.1280	768	6000	6000	197.4	.451	.722
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				146.9	.336	.538
LIVER:	1	4	9.7679	.3610	5063	14848	14620	480.9	1.100	.729
	2			.4330	6292	14531				
	3			.3240	4710	14537				
	4			.4630	6744	14566				
III. GI TRACT TISSUES										
Esophagus		1	.1566	.1566	2218	14182	14182	466.5	1.067	.011
Stomach	1	1	.9866	.9866	13540	13727	13727	451.5	1.033	.069
	2			.0000	0	0				
Sm. Intest	1	1	3.0566	3.0566	54801	17930	17930	589.8	1.349	.280
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.6485	.6485	7928	12225	12225	402.1	.920	.040
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.8203	.8203	14971	18251	18251	600.4	1.373	.076
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.5273	2.5273	15837	6266	6266	206.1	.472	.081
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.6692	.6692	7452	11136	11136	366.3	.838	.038
	2			.0000	0	0				
Prostate		1	.2222	.2222	3136	14104	14104	464.0	1.061	.016
V. OTHER TISSUES										
Trachea		1	.1502	.1502	3612	24048	24048	791.1	1.809	.018
Lungs	1	1	1.0206	1.0206	26127	25600	25600	842.1	1.926	.133
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0735	.0735	1505	20476	20476	673.6	1.541	.008
Spleen	1	1	.4586	.4586	8156	17785	17785	585.0	1.338	.042
	2			.0000	0	0				
Kidneys	1	1	1.8028	1.8028	28503	15810	15810	520.1	1.190	.145
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2821	.2821	1777	6299	6299	207.2	.474	.009
	2			.0000	0	0				
Brain	1	1	1.7503	1.7503	10288	5878	5878	193.4	.442	.052
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.7253	.7253	6182	8523	8523	280.4	.641	.032
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A28. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-151-3

TISSUE ANALYSIS

STUDY ID: CROT-4 Length (hrs): 24 Route: IV Dose date: 09-21-83 (MM-DD-YY)

ANIMAL ID: 4188-151-3 GREEN Rat Strain: F344 MALE Body Wt. (g) 232.0

DOSE Amt: 2.84 eq/kg
.660 eq Cmpd
2e7 dpm
Ref: 4188-153 Notebook-page for dose data.
Spec. Act: 30.4 dpm/ng 14C-Cmpd, ref. p. 4251-89
Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: Crot-4
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2729	6008	22015	21851	718.8	1.0000	1.597
	2			.2226	4874	21915				
	3			.2610	5680	21762				
	4			.2966	6439	21709				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.2917	2799	9595	9595	315.6	.4391	1.670
	2			.0000	0	0				
Neck	1	1	N/A	.1443	1165	8073	8073	265.6	.3695	1.405
	2			.0000	0	0				
Abdomen	1	1	N/A	.1976	1764	8927	8927	293.7	.4086	1.553
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.1283	1430	11146	11146	366.6	.5101	1.939
	2			.0000	0	0				
	AVERAGES FOR SKIN							310.4	.4318	1.642
MUSCLE:										
Neck	1	1	N/A	.3650	2429	6655	6655	218.9	.3046	3.860
	2			.0000	0	0				
Abdomen	1	1	N/A	.4161	1767	4247	4247	139.7	.1943	2.463
	2			.0000	0	0				
Hindleg	1	1	N/A	.4725	2456	5198	5198	171.0	.2379	3.015
	2			.0000	0	0				
	AVERAGES FOR MUSCLE							176.5	.2456	3.113
ADIPOSE:										
Kidney	1	1	N/A	.2338	1233	5274	5274	173.5	.2414	.612
	2			.0000	0	0				
Epididymis	1	1	N/A	.2348	950	4046	4046	133.1	.1852	.469
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2615	2325	8891	8891	292.5	.4069	1.031
	2			.0000	0	0				
	AVERAGES FOR ADIPOSE							199.7	.2778	.704
LIVER:	1	4	9.7533	.4000	4930	12325	12258	403.2	.5610	.598
	2			.3600	4486	12461				
	3			.5090	6187	12155				
	4			.4330	5235	12090				
III. GI TRACT TISSUES										
Esophagus		1	.2135	.2135	3105	15258	15258	501.9	.6983	.016
Stomach	1	1	.8725	.8725	9897	11343	11343	373.1	.5191	.049
	2			.0000	0	0				
Sm. Intest	1	1	2.9238	2.9238	39620	13551	13551	445.8	.6202	.198
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.8082	.8082	5201	6435	6435	211.7	.2945	.026
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.1470	1.1470	14357	12517	12517	411.7	.5728	.072
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.5435	2.5435	11342	4459	4459	146.7	.2041	.057
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.8164	.8164	7482	9165	9165	301.5	.4194	.037
	2			.0000	0	0				
Prostate		1	.1871	.1871	2321	12405	12405	408.1	.5677	.012
V. OTHER TISSUES										
Trachea		1	.0856	.0856	2671	31203	31203	1026.4	1.4280	.013
Lungs	1	1	1.1157	1.1157	31478	28214	28214	928.1	1.2912	.157
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0667	.0667	1292	19370	19370	637.2	.8865	.006
Spleen	1	1	.4814	.4814	10174	21134	21134	695.2	.9672	.051
	2			.0000	0	0				
Kidneys	1	1	1.7793	1.7793	21544	12108	12108	398.3	.5541	.108
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2691	.2691	1275	4738	4738	155.9	.2168	.006
	2			.0000	0	0				
Brain	1	2	.0000	.0000	0	0	0	.0	.0000	.000
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.7748	.7748	9392	12122	12122	398.7	.5548	.047
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A29. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4188-151-4

TISSUE ANALYSIS

STUDY ID: CROT-4 Length (hrs): 24 Route: IV Dose date: 09-21-83 (MM-DD-YY)

ANIMAL ID: 4188-151-4 pink Rat Strain: F344 MALE Body Wt. (g) 250.0

DOSE Amt: 2.81 mg/kg
.703 mg Cmpd
1.9%e7 dpm
Ref: 4188-153 Notebook page for dose data.
Spec. Act: 30.4 dpm/ng 14C-Cmpd; ref. p. 4251-09

Vehicle: 10% ETOH

RTI Project 311U-2227 File Name: Crot-4
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984
Compound:

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2114	4368	20662	20178	663.7	1.000	1.597
	2			.2072	4159	20072				
	3			.3070	6086	19826				
	4			.2560	5159	20152				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3100	2743	8848	8848	291.1	.439	1.667
	2			.0000	0	0				
Neck	1	1	N/A	.1920	1364	7104	7104	233.7	.352	1.339
	2			.0000	0	0				
Abdomen	1	1	N/A	.1533	989	6451	6451	212.2	.320	1.216
	2			.0000	0	0				
Hindquarters	1	1	N/A	.2311	2208	9554	9554	314.3	.474	1.800
	2			.0000	0	0				
				AVERAGES FOR SKIN				262.8	.396	1.506
MUSCLE:										
Neck	1	1	N/A	.3803	2139	5622	5622	184.9	.279	3.531
	2			.0000	0	0				
Abdomen	1	1	N/A	.7809	3512	4497	4497	147.9	.223	2.825
	2			.0000	0	0				
Hindleg	1	1	N/A	.3816	1847	4840	4840	159.2	.240	3.040
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				164.0	.247	3.132
ADIPOSE:										
Kidney	1	1	N/A	.1763	744	4220	4220	138.8	.209	.530
	2			.0000	0	0				
Epididymis	1	1	N/A	.1693	414	2445	2445	80.4	.121	.307
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2619	992	4101	4101	134.9	.203	.515
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				118.1	.178	.451
LIVER:	1	3	9.76%	.3630	5350	14738	14690	483.2	.728	.720
	2			.5070	7458	14710				
	3			.5210	7618	14622				
	4			.0000	0	0				
III. GI TRACT TISSUES										
Esophagus		1	.1620	.1620	3105	19167	19167	630.5	.950	.016
Stomach	1	1	1.0908	1.0908	10994	10079	10079	331.5	.500	.055
	2			.0000	0	0				
Sm. Intest	1	1	2.5748	2.5748	33960	13189	13189	433.9	.654	.171
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	1.1325	1.1325	6603	5813	5813	191.2	.288	.033
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	1.0760	1.0760	20090	18671	18671	614.2	.925	.101
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.4914	2.4914	13240	5314	5314	174.8	.263	.067
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.6614	.6614	5578	8434	8434	277.4	.418	.028
	2			.0000	0	0				
Prostate		1	.2798	.2798	3165	11312	11312	372.1	.561	.016
V. OTHER TISSUES										
Trachea		1	.1798	.1798	5087	28293	28293	930.7	1.402	.026
Lungs	1	1	1.0027	1.0027	30270	30188	30188	993.0	1.496	.152
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0661	.0661	1040	15734	15734	517.6	.780	.005
Spleen	1	1	.4800	.4800	8128	16933	16933	557.0	.839	.041
	2			.0000	0	0				
Kidneys	1	1	1.8510	1.8510	19454	10510	10510	345.7	.521	.098
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2348	.2348	901	3837	3837	126.2	.190	.005
	2			.0000	0	0				
Brain	1	1	1.6581	1.6581	18700	11278	11278	371.0	.559	.094
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	2	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A30. Concentration of ^{14}C in Selected Tissues 72 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-40-1

TISSUE ANALYSIS

STUDY ID: crot-7 Length (hrs): 72 Route: IV Dose date: 09-15-83 (MM-DD-YY)

ANIMAL ID: 4275-40-1 GREEN Rat Strain: F334 MALE Body Wt. (g) 299.0

DOSE Amt: 2.69 mg/kg
.804 mg Cmpd
1.4e7 dpm
Ref: 4275-49 Notebook-page for dose data.
Spec. Act: 18.2 dpm/ng 14C-Cmpd; ref. p. 4275-49
Vehicle: 10% ETOH

RTI Project 310-2227 File Name: CROT-7
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3356	1610	4797	4765	260.7	1.000	.612
	2			.2505	1190	4750				
	3			.2593	1240	4782				
	4			.2710	1260	4649				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.2139	1080	5049	5328	292.7	1.123	1.637
	2			.1559	874	5606				
Neck	1	2	N/A	.1191	364	3056	2991	164.3	.630	.919
	2			.1887	552	2925				
Abdomen	1	2	N/A	.0769	241	3134	3062	168.3	.645	.941
	2			.1809	541	2991				
Hindqtrs	1	2	N/A	.1198	412	3439	3474	190.9	.732	1.067
	2			.1160	407	3509				
				AVERAGES FOR SKIN				204.0	.783	1.141
MUSCLE:										
Neck	1	2	N/A	.2512	494	1967	1998	109.8	.421	2.046
	2			.4049	822	2030				
Abdomen	1	2	N/A	.7302	1570	2150	2232	122.7	.470	2.286
	2			.5327	1233	2315				
Hindleg	1	2	N/A	.3181	566	1779	1732	95.2	.365	1.773
	2			.3794	639	1684				
				AVERAGES FOR MUSCLE				109.2	.419	2.035
ADIPOSE:										
Kidney	1	2	N/A	.2921	318	1089	1135	62.3	.239	.232
	2			.2084	246	1180				
Epididymis	1	2	N/A	.2824	364	1289	1278	70.2	.269	.262
	2			.2045	259	1267				
Mesenteric	1	2	N/A	.1241	398	3207	3193	175.5	.673	.654
	2			.1412	449	3180				
				AVERAGES FOR ADIPOSE				102.7	.394	.383
LIVER:	1	4	10.8235	.2876	1628	5661	5758	316.3	1.213	.427
	2			.2319	1328	5727				
	3			.2675	1542	5764				
	4			.2453	1442	5879				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	.1712	.1712	1211	7074	7074	388.7	1.491	.008
Lungs	1	2	1.2781	.7077	6270	8860	8637	474.6	1.820	.076
	2			.5706	4800	8415				
	3			.0000	0	0				
Adrenals		1	.0672	.0672	669	9936	9936	546.0	2.094	.003
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A31. Concentration of ^{14}C in Selected Tissues 72 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-40-3

TISSUE ANALYSIS

STUDY ID: crot-7 Length (hrs): 72 Route: IV Dose date: 09-15-83 (MM-DD-YY)

ANIMAL ID: 4175-40-3 YELLOW Rat Strain: F334 MALE Body Wt. (g) 332.0

DOSE Amt: 2.8 mg/kg
.930 mg Cmpd
1.6Me7 dpm
Ref: 4275-49 Notebook-page for dose data.
Spec. Act: 18.2 dpm/mg 14C-Cmpd; ref. p. 4275-49
Vehicle: 10% ETOH

RTI Project 311-2227 File Name: CROT-7
Master Protocol 89 edited: 041084-PP
Today's Date: 9/15/1984 Template: Master.1
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3950	2660	7693	7724	424.4	1.0000	.956
	2			.3003	2340	7792				
	3			.2699	2120	7855				
	4			.2450	1900	7755				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1773	822	4636	4843	266.1	.6270	1.427
	2			.1398	706	5050				
Neck	1	2	N/A	.2994	1680	5611	4880	268.1	.6318	1.438
	2			.1998	829	4149				
Abdomen	1	2	N/A	.1594	611	3833	4046	222.3	.5238	1.192
	2			.0742	316	4259				
Hindqtrs	1	2	N/A	.1986	801	4033	3643	200.2	.4717	1.074
	2			.0962	313	3254				
		AVERAGES FOR SKIN						239.2	.5636	1.283
MUSCLE:										
Neck	1	2	N/A	.4224	1060	2509	2621	144.0	.3393	2.574
	2			.3064	837	2732				
Abdomen	1	2	N/A	.4563	1350	2959	2983	163.9	.3862	2.930
	2			.3891	1170	3007				
Hindleg	1	2	N/A	.3922	756	1925	2002	110.0	.2592	1.967
	2			.3352	697	2079				
		AVERAGES FOR MUSCLE						139.3	.3282	2.490
ADIPOSE:										
Kidney	1	2	N/A	.3859	306	793	838	46.1	.1085	.165
	2			.4019	355	883				
Epididymis	1	2	N/A	.2140	185	864	862	47.4	.1116	.169
	2			.2875	247	859				
Mesenteric	1	2	N/A	.1401	262	1870	1934	106.2	.2503	.380
	2			.1337	267	1997				
		AVERAGES FOR ADIPOSE						66.5	.1568	.238
LIVER:	1	4	12.1788	.2289	1238	5408	5378	295.5	.6963	.388
	2			.2214	1196	5402				
	3			.2419	1279	5287				
	4			.2344	1269	5414				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	.2380	.2380	2170	9118	9118	501.0	1.1805	.013
Lungs	1	2	1.2269	.5229	5110	9772	9979	548.3	1.2919	.072
	2			.7040	7170	10185				
	3			.0000	0	0				
Adrenals		1	.0676	.0676	567	8388	8388	460.9	1.0859	.003
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A32. Concentration of ^{14}C in Selected Tissues 72 h after Intravenous Administration of [^{14}C]Crotonaldehyde to Rat 4275-40-4

TISSUE ANALYSIS

STUDY ID: crot-7 Length (hrs): 72 Route: IV Dose date: 09-15-83 (MM-DD-YY)

ANIMAL ID: 4275-40-4 BLUE Rat Strain: F334 MALE Body Wt. (g) 307.0

DOSE Amt: 2.91 mg/kg
.893 mg Cmpd
1.62e7 dpm
Ref: 4275-49 Notebook-page for dose data.
Spec. Act: 18.2 dpm/ng 14C-Cmpd, ref. p. 4275-49
Vehicle: 10% ETOH

RTI Project 311-2227 File Name: CROT-7
Master Protocol 89 edited: 04108A-PP
Today's Date: 9/15/1984 Template: 0
Compound: Crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2870	2230	7770	7789	428.0	1.000	.930
	2			.1712	1320	7710				
	3			.2650	2070	7811				
	4			.1755	1380	7863				
II. MAJOR TISSUES										
SKIN:										
Ear	1	2	N/A	.1289	568	4407	4258	234.0	.547	1.210
	2			.1280	526	4109				
Neck	1	2	N/A	.1833	459	2504	2676	147.0	.344	.761
	2			.1166	332	2847				
Abdomen	1	2	N/A	.1900	494	2600	2807	154.2	.360	.798
	2			.1798	542	3014				
Hindlmbs	1	2	N/A	.2362	818	3463	3584	196.9	.460	1.019
	2			.1941	719	3704				
		AVERAGES FOR SKIN						183.0	.428	.947
MUSCLE:										
Neck	1	2	N/A	.2809	582	2072	2029	111.5	.261	1.923
	2			.2738	544	1987				
Abdomen	1	2	N/A	.3107	578	1860	2070	113.7	.266	1.961
	2			.3602	821	2279				
Hindleg	1	2	N/A	.4236	648	1530	1604	88.1	.206	1.520
	2			.3786	635	1677				
		AVERAGES FOR MUSCLE						104.5	.244	1.801
ADIPOSE:										
Kidney	1	2	N/A	.2251	241	1071	1049	57.6	.135	.199
	2			.2141	220	1028				
Epididyeis	1	1	N/A	.0000	0	0	1705	93.7	.219	.323
	2			.2504	427	1705				
Mesenteric	1	2	N/A	.1539	359	2333	2727	149.8	.350	.517
	2			.1301	406	3121				
		AVERAGES FOR ADIPOSE						100.4	.235	.346
LIVER:	1	4	11.3361	.2077	1002	4824	4849	266.5	.623	.339
	2			.2369	1157	4884				
	3			.2931	1421	4848				
	4			.2460	1191	4841				
III. GI TRACT TISSUES										
Esophagus		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Stomach	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Sm. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Cecum	1	3	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
Lg. Intest	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
(B)	1			N/A	N/A	N/A				
	2			N/A	N/A	N/A				
Sem. Ves.	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Prostate		1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
V. OTHER TISSUES										
Trachea		1	.1954	.1954	1755	8982	8982	493.5	1.153	.011
Lungs	1	2	1.3373	.5609	5120	9128	8911	489.6	1.144	.074
	2			.7764	6750	8694				
	3			.0000	0	0				
Adrenals		1	.0225	.0225	246	10933	10933	600.7	1.404	.002
Spleen	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Kidneys	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Eyes	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
Brain	1	4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				
	3			N/A	N/A	N/A				
	4			N/A	N/A	N/A				
Heart	1	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2			N/A	N/A	N/A				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A33. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde in 2% EtOH to Rat 4188-151-2

TISSUE ANALYSIS

STUDY ID: Crot-5 Length (hrs): 24 Route: IV Dose date: 09-21-83 (MM-DD-YY)

ANIMAL ID: 4188-152-2 RED Rat Strain: F344 MALE Body Wt. (g) 230.0

DOSE Amt: 2.89 mg/kg
.665 mg Cmpd
4.82e6 dpm
Ref: 4188-153 Notebook-page for dose data.
Spec. Act: 7.25 dpm/ng 14C-Cmpd, ref. p. 4251-69
Vehicle: 2% ETOH

RTI Project 311U-2227 File Name: CROT-5
Master Protocol 69 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound: crotonaldehyde

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eqv Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2061	1046	5075	5067	698.8	1.000	1.523
	2			.1265	698	5518				
	3			.1969	923	4688				
	4			.2788	1390	4986				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.2930	613	2092	2092	288.6	.413	1.497
	2			.0000	0	0				
Neck	1	1	N/A	.1525	287	1882	1882	259.6	.371	1.347
	2			.0000	0	0				
Abdomen	1	1	N/A	.1727	405	2345	2345	323.5	.463	1.679
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.1136	336	2958	2958	408.0	.584	2.117
	2			.0000	0	0				
AVERAGES FOR SKIN								319.9	.458	1.660
MUSCLE:										
Neck	1	1	N/A	.4820	732	1519	1519	209.5	.300	3.623
	2			.0000	0	0				
Abdomen	1	1	N/A	.5028	559	1112	1112	153.3	.219	2.653
	2			.0000	0	0				
Hindleg	1	1	N/A	.6928	802	1158	1158	159.7	.228	2.762
	2			.0000	0	0				
AVERAGES FOR MUSCLE								174.2	.249	3.013
ADIPOSE:										
Kidney	1	1	N/A	.2452	307	1252	1252	172.7	.247	.997
	2			.0000	0	0				
Epididymis	1	1	N/A	.3423	181	529	529	72.9	.104	.252
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2778	529	1904	1904	262.7	.376	.909
	2			.0000	0	0				
AVERAGES FOR ADIPOSE								169.4	.242	.586
LIVER:	1	4	9.2665	.3360	1448	4310	4302	593.3	.849	.825
	2			.2690	1065	4277				
	3			.3550	1522	4287				
	4			.3190	1392	4332				
III. GI TRACT TISSUES										
Esophagus		1	.1840	.1840	1845	10027	10027	1383.1	1.979	.038
Stomach	1	1	1.3377	1.3377	3461	2587	2587	356.9	.511	.072
	2			.0000	0	0				
Sm. Intest	1	1	2.6962	2.6962	7335	2720	2720	375.2	.537	.152
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	1.1697	1.1697	2156	1841	1841	254.0	.363	.045
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	4	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.2083	2.2083	2862	1296	1296	178.8	.256	.059
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.6800	.6800	1489	2190	2190	302.0	.432	.031
	2			.0000	0	0				
Prostate		1	.3710	.3710	537	1447	1447	199.6	.286	.011
V. OTHER TISSUES										
Trachea		1	.1508	.1508	984	6525	6525	900.0	1.288	.020
Lungs	1	1	.9951	.9951	7169	7204	7204	993.7	1.422	.149
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0647	.0647	345	5332	5332	735.5	1.052	.007
Spleen	1	1	.5113	.5113	2217	4336	4336	598.1	.856	.046
	2			.0000	0	0				
Kidneys	1	1	1.8829	1.8829	5905	3136	3136	432.6	.619	.123
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2507	.2507	357	1424	1424	196.4	.281	.007
	2			.0000	0	0				
Brain	1	1	1.6093	1.6093	3621	2250	2250	310.4	.444	.075
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.757%	.757%	1692	2234	2234	308.1	.441	.035
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A34. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde in 2% EtOH to Rat 4188-152-3

TISSUE ANALYSIS

STUDY ID: Crot-5 Length (hrs): 24 Route: IV Dose date: 09-21-83 (MM-DD-YY)

ANIMAL ID: 4188-152-3 white Rat Strain: F334 MALE Body Wt. (g) 232.0

DOSE Act: 2.8 mg/kg .650 mg Cmpd 4.7146 dpm Vehicle: 2% ETOH

Ref: 4188-153 Notebook-page for dose data.
Spec. Act: 7.25 dpm/ng 14C-Cmpd; ref. p. 4251-69

RTI Project 311U-2227 File Name: CROT-5
Master Protocol 69 edited: DA10B4-PP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No. of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	ng-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.2326	1433	6161	6599	910.2	1.0000	2.048
	2			.2782	2058	7398				
	3			.3712	2334	6288				
	4			.3013	1973	6548				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.2427	685	2822	2822	389.3	.4277	2.085
	2			.0000	0	0				
Neck	1	1	N/A	.2150	452	2102	2102	290.0	.3186	1.553
	2			.0000	0	0				
Abdomen	1	1	N/A	.2352	818	3478	3478	479.7	.5271	2.570
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.2100	563	2681	2681	369.8	.4063	1.981
	2			.0000	0	0				
				AVERAGES FOR SKIN				382.2	.4199	2.047
MUSCLE:										
Neck	1	1	N/A	.5088	677	1331	1331	183.5	.2016	3.277
	2			.0000	0	0				
Abdomen	1	1	N/A	.5283	712	1348	1348	185.9	.2042	3.319
	2			.0000	0	0				
Hindleg	1	1	N/A	.5796	708	1222	1222	168.5	.1851	3.008
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				179.3	.1970	3.202
ADIPOSE:										
Kidney	1	1	N/A	.3231	732	2266	2266	312.5	.3433	1.116
	2			.0000	0	0				
Epididymis	1	1	N/A	.1716	231	1346	1346	185.7	.2040	.663
	2			.0000	0	0				
Mesenteric	1	1	N/A	.2138	988	4621	4621	637.4	.7003	2.276
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				378.5	.4159	1.352
LIVER:	1	4	8.9375	.3940	1338	3484	3546	489.1	.5374	.673
	2			.5100	1802	3533				
	3			.5670	2099	3576				
	4			.4300	1544	3991				
III. GI TRACT TISSUES										
Esophagus		1	.1927	.1927	855	4437	4437	612.0	.6724	.018
Stomach	1	1	1.1350	1.1350	3949	3479	3479	479.9	.5273	.084
	2			.0000	0	0				
Sm. Intest	1	1	2.9285	2.9285	10837	3701	3701	510.6	.5608	.230
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecus	1	1	.8040	.8040	1783	2218	2218	305.9	.3361	.038
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.8656	.8656	3632	4196	4196	578.7	.6359	.077
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.4549	2.4549	3300	1344	1344	185.4	.2037	.070
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.2822	.2822	653	2314	2314	319.2	.3507	.014
	2			.0000	0	0				
Prostate		1	.2247	.2247	640	2848	2848	392.9	.4316	.014
V. OTHER TISSUES										
Trachea		1	.1277	.1277	1359	10642	10642	1467.9	1.6128	.029
Lungs	1	1	1.0903	1.0903	8387	7692	7692	1061.0	1.1658	.178
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0563	.0563	386	6856	6856	945.7	1.0390	.008
Spleen	1	1	.5770	.5770	3038	5265	5265	726.2	.7979	.065
	2			.0000	0	0				
Kidneys	1	1	1.7772	1.7772	6437	3622	3622	499.6	.5489	.137
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2597	.2597	402	1548	1548	213.5	.2346	.009
	2			.0000	0	0				
Brain	1	1	1.6729	1.6729	4266	2550	2550	351.7	.3865	.091
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	1	.6966	.6966	1678	2409	2409	332.3	.3651	.036
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.

Table A35. Concentration of ^{14}C in Selected Tissues 24 h after Intravenous Administration of [^{14}C]Crotonaldehyde in 2% EtOH to Rat 4188-152-4

TISSUE ANALYSIS

STUDY ID: Crot-5 Length (hrs): 24 Route: IV Dose date: 09-21-83 (MM-DD-YY)

ANIMAL ID: 4188-152-4 orange Rat Strain: F334 MALE Body Wt. (g) 229.0

DOSE Amt: 2.84 mg/kg
650.340 mg Cmpd
4.7146 dpm
Ref: 4188-153 Notebook-page for dose data.
Spec. Act: 7.25 dpm/mg 14C-Cmpd; ref. p. 4251-69

RTI Project 310-2227 File Name: CROT-5
Master Protocol 89 edited: 041084-PP
Today's Date: 9/ 8/1984
Compound:

TISSUE		No.of Aliquots taken	Total Organ Wt. (g)	Aliquot Wt. (g)	Total DPM per Aliquot	DPM/g Tissue	Avg DPM/g Tissue	mg-eq Cmpd per g Tissue	TBR	% Dose in Total Tissue
I. BLOOD	1	4	N/A	.3360	1989	5920	5349	737.8	1.000	1.638
	2			.2873	1624	5653				
	3			.3531	1761	4987				
	4			.4064	1956	4837				
II. MAJOR TISSUES										
SKIN:										
Ear	1	1	N/A	.3617	876	2564	2564	353.6	.479	1.870
	2			.0000	0	0				
Neck	1	1	N/A	.4062	991	2440	2440	336.5	.456	1.779
	2			.0000	0	0				
Abdomen	1	1	N/A	.2118	670	3163	3163	436.3	.591	2.307
	2			.0000	0	0				
Hindqtrs	1	1	N/A	.2579	823	3191	3191	440.2	.597	2.327
	2			.0000	0	0				
				AVERAGES FOR SKIN				391.7	.531	2.071
MUSCLE:										
Neck	1	1	N/A	.5123	967	1888	1888	260.4	.353	4.589
	2			.0000	0	0				
Abdomen	1	1	N/A	.6641	950	1431	1431	197.3	.267	3.478
	2			.0000	0	0				
Hindleg	1	1	N/A	.9956	642	1078	1078	148.7	.202	2.620
	2			.0000	0	0				
				AVERAGES FOR MUSCLE				202.1	.274	3.562
ADIPOSE:										
Kidney	1	1	N/A	.3123	508	1627	1627	224.4	.304	.791
	2			.0000	0	0				
Epididymis	1	1	N/A	.2526	389	1540	1540	212.4	.288	.749
	2			.0000	0	0				
Mesenteric	1	1	N/A	.1752	507	2894	2894	399.1	.541	1.407
	2			.0000	0	0				
				AVERAGES FOR ADIPOSE				278.6	.378	.982
LIVER:	1	4	10.1381	.2970	1143	3848	3835	529.0	.717	.826
	2			.4480	1706	3804				
	3			.5420	2086	3849				
	4			.4530	1740	3841				
III. GI TRACT TISSUES										
Esophagus		1	.2631	.2631	1566	5952	5952	821.0	1.113	.033
Stomach	1	1	1.1597	1.1597	2698	2326	2326	320.9	.435	.057
	2			.0000	0	0				
Sm. Intest	1	1	2.5788	2.5788	8391	3254	3254	448.8	.608	.178
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Cecum	1	1	.9982	.9982	1992	1996	1996	275.3	.373	.042
	2			.0000	0	0				
	3			.0000	0	0				
Lg. Intest	1	1	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
IV. REPRODUCTIVE TISSUES										
Testes (A)	1	1	2.3726	2.3726	2593	1093	1093	150.7	.206	.055
	2			.0000	0	0				
(B)	1			.0000	0	0				
	2			.0000	0	0				
Sem. Ves.	1	1	.7292	.7292	1720	2359	2359	325.3	.441	.037
	2			.0000	0	0				
Prostate		1	.2984	.2984	953	3194	3194	440.5	.597	.020
V. OTHER TISSUES										
Trachea		1	.0668	.0668	392	5868	5868	809.4	1.097	.008
Lungs	1	1	1.2113	1.2113	7605	6278	6278	866.0	1.174	.161
	2			.0000	0	0				
	3			.0000	0	0				
Adrenals		1	.0573	.0573	318	5550	5550	765.5	1.038	.007
Spleen	1	1	.4850	.4850	2006	4136	4136	570.5	.773	.043
	2			.0000	0	0				
Kidneys	1	1	1.8448	1.8448	4853	2631	2631	362.8	.492	.103
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Eyes	1	1	.2277	.2277	430	1888	1888	260.5	.353	.009
	2			.0000	0	0				
Brain	1	1	1.5692	1.5692	4166	2655	2655	366.2	.496	.088
	2			.0000	0	0				
	3			.0000	0	0				
	4			.0000	0	0				
Heart	1	2	.0000	.0000	0	0	0	.0	.000	.000
	2			.0000	0	0				

1. TBR = Tissue:Blood Ratio
2. Total organ weight is the sum of the aliquot weights for all tissues except blood, skin, muscle, adipose and liver.
3. Blood is assumed to be 6.3% of total body weight; skin 15%, muscle 50% and adipose 10%.
4. The liver is weighed, homogenized and aliquots are taken for oxidation.