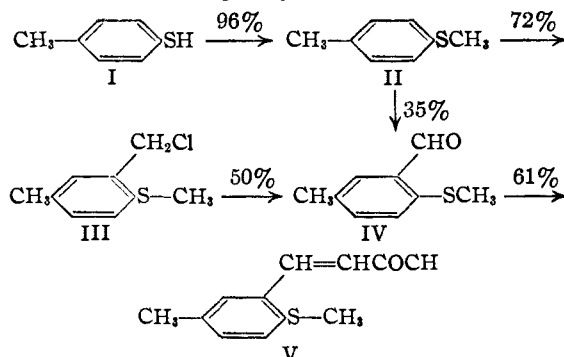


Syntheses of 2-Methylmercapto-5-methylbenzaldehyde and 2-Methylmercapto-5-methylcinnamic Acid

BY EDWARD G. HOWARD, E. CAMPAIGNE AND R. L. SHRINER

In experiments designed to synthesize 6-methylthiocoumarin, 2-methylmercapto-5-methylcinnamic acid (V) was synthesized from 2-methylmercapto-5-methylbenzaldehyde (IV). The latter compound was prepared indirectly by methylation of *p*-thiocresol (I), followed by chloromethylation and conversion of the chloromethyl compound (III) to the aldehyde (IV) by means of the Sommelet reaction. The aldehyde (IV) was also made from methyl *p*-tolyl sulfide (II) by the Gattermann procedure. The Knoevenagel condensation of IV with malonic acid gave the substituted cinnamic acid V in good yields.



Efforts to cleave the thioether linkage in V, were unsuccessful. Cyanogen bromide, ordinarily a convenient reagent for cleavage of thioethers,¹ did not react under mild conditions, and caused complete decomposition of the molecule under more drastic conditions.

Experimental²

Methyl *p*-Tolyl Sulfide (II).—This was prepared by direct methylation of *p*-thiocresol with methyl sulfate, as described by Auwers and Arndt.³ From 124 g. (1.0 mole) of *p*-thiocresol was obtained 130 g. (96%) of methyl *p*-tolyl sulfide, b. p. 102° (20 mm.).

2-Methylmercapto-5-methylbenzyl Chloride (III).—This compound was previously reported by Brunner⁴ but no specific directions were given.

Into a 500-ml. three-necked flask fitted with a stirrer, thermometer and gas inlet tube was placed 42.0 g. (0.3 mole) of *p*-thiocresol methyl ether, 24.8 g. (0.33 mole) of 40% formaldehyde solution and 220 g. of concentrated hydrochloric acid. The stirred mixture was cooled to 10°, and dry hydrogen chloride gas was bubbled through the mixture for three hours, after which the temperature was permitted to rise to 20° and kept there for two hours longer. Finally it was heated to 67–71° for four hours. After cooling, the product was removed from the reaction mixture by extraction with petroleum ether. The combined extracts were dried over anhydrous calcium chloride. The product was vacuum distilled giving these fractions: Fraction I, b. p. (6 mm.) 116–124°, 9 g.; fraction II,

b. p. (6 mm.) 124–127°, 40 g. (Brunner gives a boiling point of 132–134° at 6 mm. and a melting point of 31°.) Both fractions melted at 30°. The yield based on fraction II is 72% of the theoretical amount, and 88% when based on both fractions.

2-Methylmercapto-5-methylbenzaldehyde (IV).—A mixture of 9.0 g. (0.049 mole) of III, 9 g. (0.064 mole) of hexamethylenetetramine, and 160 ml. of chloroform was refluxed for twenty-four hours, the solvent removed, and the resulting product refluxed with 100 ml. of 20% hydrochloric acid for one-half hour. This mixture was cooled, extracted with ether, and the combined ether extracts washed with water until neutral. After drying over anhydrous calcium sulfate, the ether was removed and the resulting yellow oil distilled, b. p. 129–134° (3.5 mm.), yield 4.1 g. (50%).

*Anal.*⁵ Calcd. for C₁₀H₁₀OS: S, 19.27. Found: S, 19.34.

The 2,4-dinitrophenylhydrazone was prepared and recrystallized from xylene. It consisted of orange needles, m. p. 254°.

Anal. Calcd. for C₁₅H₁₄O₄N₂S: N, 16.2. Found: N, 16.5.

This aldehyde was also prepared from methyl *p*-tolyl sulfide by the Gattermann reaction with zinc cyanide, hydrogen chloride and aluminum chloride, as described by Adams⁶ for phenolic ethers, but the yield was only 35% and the reaction is less convenient.

2-Methylmercapto-5-methylcinnamic Acid (V).—The crude aldehyde (IV), 18 g. (0.11 mole), was heated at 70° for four hours with 11.4 g. (0.11 mole) of malonic acid, 10.2 g. (0.11 mole) of α -picoline, and 0.5 ml. of piperidine. After cooling, the reaction mixture was dissolved in ether and extracted with 10% hydrochloric acid to remove the amines, and then with 2 *N* sodium hydroxide. Upon acidification of the basic extracts, a yellow solid precipitated which was recrystallized from alcohol. It weighed 14 g., (0.067 mole, 61%) m. p. 154–155.5°.

Anal. Calcd. for C₁₁H₁₂O₂S: S, 15.39. Found: S, 15.46.

(5) We are indebted to R. Clifford Bourgeois for this analysis.

(6) Adams and Levine, *THIS JOURNAL*, **45**, 2373 (1923); Adams and Montgomery, *ibid.*, **46**, 1518 (1924).

DEPARTMENT OF CHEMISTRY
INDIANA UNIVERSITY

BLOOMINGTON, INDIANA

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The Separation of Nuclear Isomers of Bromine on Silver Plates

By W. S. Koski¹

If bromine nuclei are irradiated with slow neutrons, two radioactive nuclei, Br⁸⁰ and Br⁸² are formed. Br⁸² decays with a 34-hour period, and Br⁸⁰ is a nuclear isomer which decays by gamma emission from a metastable state with a 4.4-hr. period to a ground state of the same nucleus. The ground state of Br⁸⁰ then decays with an 18-min. period β disintegration to Kr⁸⁰. As a result of the isomeric transition the bromine possesses unusual chemical reactivity, and by utilizing this property Roussinow and Karamian^{2,3} were able to separate the genetically related nuclear isomers of bromine. Their results have prompted the

(1) Present address: Department of Chemistry, The Johns Hopkins University, Baltimore, Md.

(2) L. I. Roussinow and A. S. Karamian, *Acad. Sci. URSS*, **55** (no. 7), 603–605 (1947).

(3) A. S. Karamian and L. I. Roussinow, *ibid.*, **58** (no. 4), 573–574 (1947).

(1) v. Braun, May and Michaelis, *Ann.*, **490**, 189 (1931).

(2) All melting points are uncorrected.

(3) Auwers and Arndt, *Ber.*, **42**, 537 (1909).

(4) Brunner, *Chem. Zentr.*, **103**, I, 2997 (1932); U. S. Patent 1,887,396 (1933); *C. A.*, **27**, 1359 (1933).

writer to report on an interrupted investigation which has direct bearing on this subject. The results reported here are essentially compatible with their work.

A fraction of redistilled *n*-butyl bromide (Eastman Kodak Co.) boiling between 101–102° (corrected to sea level) was irradiated with slow neutrons in the thermal column of the Los Alamos water boiler for two hours and, after removal, it was permitted to stand until transient equilibrium between the trace amounts of 4.4-hr. Br^{80*} (* indicates metastable state) and 18-min. Br^{80} was established. No attempt was made to clean up or purify the sample after irradiation. The sample was then dissolved in about ten times its volume of acetone. A pair of silver electrodes separated by a distance of about 4 mm. and held at a potential difference of ten volts was placed into the solution 10 min. after dilution. The electrodes were removed after 15 sec. of immersion, washed in acetone for about the same period of time, dried and then measured for activity with a Geiger-Mueller counter. It was found that both electrodes had adsorbed radioactivity, and a study of the decay curve showed that there was an enrichment of the 18-min. bromine over the equilibrium value. The anode had an activity greater by a factor of ten than the cathode. Increasing the voltage gave greater activity and more efficient separation on the anode.

The fact that the bromine isomers can be separated in the above manner is rather interesting

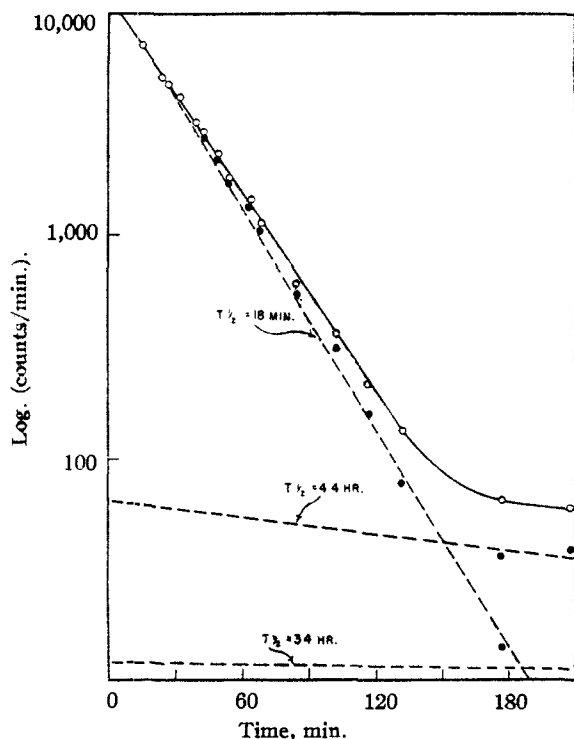


Fig. 1.—Decay curve of bromine activity picked up by silver foil.

since it indicates that at least an appreciable fraction of the 18-min. isomer appears as negative ions. Since it is not very likely that the bromine would become negatively charged during the course of the isomeric transition, it is probable that it obtains its charge through some secondary process such as chemical reaction with either its neighboring butyl bromide molecules or with some impurity. If this is the case, the 18-min. bromine possesses unusual chemical reactivity immediately after the isomeric transition, and one might expect to be able to perform an isomer separation based on this enhanced reactivity.

To test this idea, a portion of the same butyl bromide sample was irradiated in the thermal neutron flux of the reactor. Again no attempt was made to purify the sample after irradiation. Eighteen hours after bombardment the sample was dissolved in acetone and 10 min. later a silver foil was immersed in the solution for 15 sec., then the foil was removed and vigorously stirred in acetone for 15 seconds, dried and measured for activity. A typical result is shown in Fig. 1 where the logarithm of the activity is plotted against the time in minutes. The broken lines show a breakdown of the experimentally obtained curve into an 18-min. period and a long-lived 4.4-hr. Br^{80*} (* indicates metastable state) in equilibrium with 18-min. Br^{80} and 34-hr. Br^{82} . It is clear that an appreciable enrichment of the short lived isomer had been obtained.

It is expected that the ratio of extrapolated activities of the 4.4-hr. bromine and 34-hr. bromine be the same as the inverse ratio of their half lives. This is roughly the case (5.5 compared to 7.7). The difference is not believed to be significant since the measured activity of the 34-hr. bromine corresponded to only a few counts above background which was rather large (50 counts/min.), consequently, the error may be large.

The amount of long lived radiobromine in any one experiment can be reduced by repeated washings with acetone. However, in no case was complete removal of the long lived material accomplished by such treatment.

For a potential difference of ten volts between foils, roughly the same separation efficiencies were obtained with charged and uncharged foils if the separation was made in the same solution and the measurements were referred to a common time. This observation indicates that the separation effect is predominantly chemical, although the yield of deposit depends on charge. The various factors that affect both the electrical and chemical methods of isomer separation will be investigated in future work.

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