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

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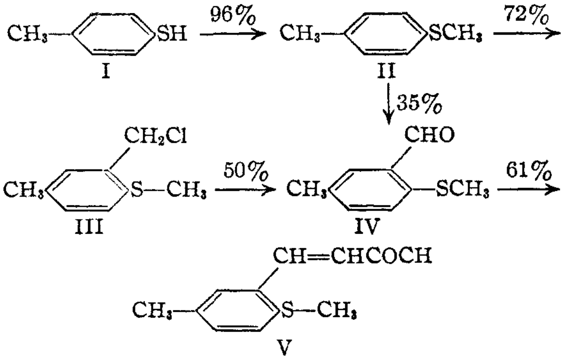
In experiments designed to synthesize 6-methylthiocoumarin, 2-methylmercapto-5-methylcinnamic acid (V) was synthesized from 2-methylmercapto-5-methylbenzaldehyde (IV). The latter compound was prepared indirectly by methylation of *p*-thiocresol (I), followed by chloromethylation and conversion of the 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.

Experimental[2]

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 Brunner[4] 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 150 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 $C_9H_{10}OS$: 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 $C_{15}H_{14}O_4N_4S$: N, 16.2. Found: N, 16.5.

This aldehyde was also prepared from methyl *p*-tolyl sufide by the Gattermann reaction with zinc cyanide, hydrogen chloride and aluminum chloride, as described by Adams[6] 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 $C_{11}H_{12}O_2S$: S, 15.39. Found: S, 15.46.

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(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).

(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).

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The Separation of Nuclear Isomers of Bromine on Silver Plates

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If bromine nuclei are irradiated with slow neutrons, two radioactive nuclei, Br^{80} and Br^{82} are formed. Br^{82} decays with a 34-hour period, and Br^{80} 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 Br^{80} then decays with an 18-min. period β disintegration to Kr^{80}. 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

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(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).