

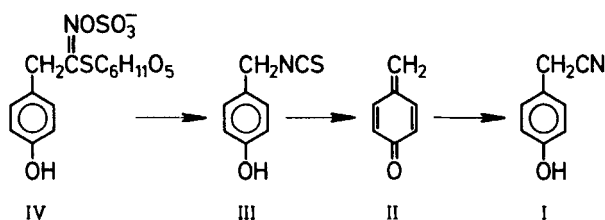
YELLOW MUSTARD OIL AS A LATENT QUINONE METHIDE: A CONVENIENT
PREPARATION OF *p*-HYDROXYBENZYL [^{14}C]CYANIDE

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Summary: Naturally derived *p*-hydroxybenzyl isothiocyanate, a hitherto
unconsidered example of the rare class of stable *p*-hydroxybenzylating agents,
was used for preparation of labelled *p*-hydroxybenzyl cyanide.

Keywords: *p*-Hydroxybenzylation, quinone methides, mustard oils, crown ethers.

Labelled *p*-hydroxybenzyl cyanide (I) has been used in several
experiments on biosynthesis of tyrosine-derived cyanogenic gluco-
sides. However, methods described in the literature¹⁻³ for pre-
paration of ^{14}C -labelled I lack simplicity. Therefore we devised
a new, more convenient procedure for preparation of this material
for our studies.



Benzyl cyanides are normally obtained from the corresponding
halides and alkali metal cyanides.⁴ However, *p*-hydroxybenzyl
halides, which are immediate precursors of 4-methylene-2,5-cyclo-
hexadien-1-one (quinone methide,⁵ II), have apparently never been
isolated owing to their instability,⁶ and hence protected or less
reactive substrates must be used.^{2,7,8} We found that stable^{9,10}
p-hydroxybenzyl isothiocyanate (mustard oil of yellow mustard,¹¹
III) reacts instantly at room temperature with potassium cyanide
solubilized in acetonitrile by 18-crown-6 to give I. The mustard

oil III is readily available from seeds of *Sinapis alba* L. (common yellow mustard), which contain large amounts of glucosinolate IV, hydrolyzed by associated thioglucosidases to give III.^{12,13}

By this means labelled I was prepared from [¹⁴C]cyanide in a radiochemical yield of 44%. Evidently I could be obtained from [¹³C] or [¹⁵N]cyanide with like efficiency. In our opinion III, which reacts in basic medium as a *p*-hydroxybenzyl halide, will prove to be a generally useful reagent for one-step *p*-hydroxybenzylation.

p-HYDROXYBENZYL ISOTHIOCYANATE (III). Yellow mustard flour (defatted with petroleum ether; 150 g) was extracted with three 500-ml portions of boiling 90% methanol and the extracts evaporated almost to dryness *in vacuo*. The resulting crude glucosinolate (IV) was dissolved in 1 liter of 0.2 M phosphate buffer (pH 5.5), 1 g of defatted mustard flour and 100 mg of ascorbic acid added, and the solution covered with 1 liter of ether and stirred for 2 h at room temperature. The ether layer was separated, the aqueous solution extracted with two 500-ml portions of ether, and the extracts dried (MgSO₄) and evaporated. The crude mustard oil was purified by column chromatography on silica gel in ether-pentane (1:1) to give 3.5 g of III; m.p. 41-42°C (from pentane; lit.^{9,10} m.p. 42°C); ν_{max}^{KBr} 3350, 2175, 2095 cm⁻¹; δ^{CDCl_3} 4.64 (CH₂), 5.3-5.4 (OH), 6.7-7.3 (C₆H₄) ppm.

p-HYDROXYBENZYL CYANIDE (I). To a solution of 60 mg of KCN (0.92 mmol) and 0.5 g of 18-crown-6 (1.9 mmol) in 20 ml of acetonitrile, a solution of 100 mg of III (0.605 mmol) in 2 ml of acetonitrile was added in one portion. After 5 minutes the solution was evaporated and the residue chromatographed in ether on a silica gel column to give 70 mg (87% from III) of I; m.p. 70-71°C (from ether-pentane); identity confirmed by IR and ¹H NMR spectra.

p-HYDROXYBENZYL [¹⁴C]CYANIDE (I). To a solution of 3 mg of KCN (520 μCi) and 30 mg of 18-crown-6 in 2 ml of acetonitrile, a solution of 5 mg of III in 0.2 ml of acetonitrile was added. After addition of 5 mg of cold I, the solution was applied to a preparative TLC plate (silica gel) and the plate developed twice with ether-pentane-acetic acid (20:20:1). The areas containing I were located under UV light and the product extracted with ether, an additional 5 mg of cold I being added during the isolation. Yield 11.5 mg of crystalline I (230 μCi or 44% radiochemical yield). The radiochemical purity of the product was confirmed by TLC in several solvent systems followed by scanning or autoradiography.

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