

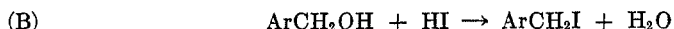
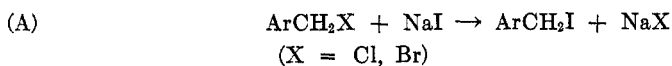
THE SYNTHESIS OF SOME SUBSTITUTED BENZYL IODIDES<sup>1</sup>

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A number of substituted benzyl iodides have been synthesized for use in studies on the exchange of benzyl type iodides with radioactive iodide ion. These exchange studies are being carried out by M. Kahn and co-workers in this laboratory.

Two different methods (A and B) were used for the preparation of the iodides. In Procedure A the corresponding chloride or bromide was allowed to exchange with sodium iodide in dry acetone and Procedure B consisted of treating the corresponding arylcarbinol with hydriodic acid.



The benzyl iodides prepared are shown in Table I. Using procedure A, the reaction was usually allowed to proceed for a half to one hour at 30 to 50°, and, after removing the resulting sodium bromide or chloride, the acetone was concentrated and cooled (Aa) or removed completely (Ab). In procedure B the carbinol was treated with 57 % hydriodic acid, the flask shaken and then chilled for an hour.

Procedure A was also used to prepare 4-iodomethyl-2-phenyl-1,2,3,2*H*-triazole (83 % yield), 1-iodomethylnaphthalene, and 2-iodomethylnaphthalene. The last two compounds decomposed to black tars before they could be isolated in pure form. *m*-Methylbenzyl iodide and *p*-ethylbenzyl iodide were liquids which decomposed readily with the liberation of free iodine. An attempt to prepare 4-iodocinnoline from 4-chlorocinnoline using Procedure A failed, 4-chlorocinnoline being recovered unchanged.

EXPERIMENTAL<sup>2, 3</sup>

*p*-Fluorobenzyl iodide. *Procedure A.* A solution of 85.7 g. (0.454 mole) of *p*-fluorobenzyl bromide (11), b.p. 93–94° at 23 mm., in 150 ml. of dry acetone was added to a solution of 69.5 g. (0.464 mole) of sodium iodide in 250 ml. of dry acetone in a one liter round-bottomed flask. The flask was stoppered and allowed to stand at room temperature for 24 hours, after which time the precipitated sodium bromide was removed. The acetone was removed from the resulting solution by distillation and the residue was taken up in benzene. The red benzene solution was washed with 5% sodium thiosulfate, which removed the red color, and dried over calcium chloride. Distillation of this solution through a 24-inch Vigreux

<sup>1</sup> This work was carried out under the auspices of the Atomic Energy Commission and the Los Alamos Scientific Laboratory.

<sup>2</sup> All melting points are uncorrected.

<sup>3</sup> All of the iodides are powerful lachrymators with the lower melting ones being the most effective.

TABLE I  
SUBSTITUTED BENZYL IODIDES  $\text{RC}_6\text{H}_4\text{CH}_2\text{I}$  OR  $\text{R}_2\text{C}_6\text{H}_3\text{CH}_2\text{I}$

R	Procedure	Crude Yield, %	Recryst. Solvent	Appearance	M.P., °C.	Formula	Iodine Analysis	
							Calc'd	Found
<i>p</i> -F	A	58	Hexane	Pale yellow rods	34-35	$\text{C}_7\text{H}_6\text{FI}$	53.77	53.85
<i>p</i> -Cl	Aa <sup>a</sup>	57	Pet. ether	Colorless needles	62-63 <sup>b</sup>	$\text{C}_7\text{H}_5\text{ClI}$	50.25	49.74
<i>p</i> -Br	Aa <sup>c</sup>	53	Pet. ether	Pale yellow needles	73-74 <sup>d</sup>	$\text{C}_7\text{H}_4\text{BrI}$	42.73	42.57
<i>p</i> -I	Aa <sup>e</sup>	57	Ethanol	Pale yellow needles	85.5-86.5	$\text{C}_7\text{H}_5\text{I}_2$	36.89 <sup>f</sup>	36.92
3,4-diCl	Ab <sup>g</sup>	70	Ethanol	Colorless needles	57-58	$\text{C}_7\text{H}_3\text{Cl}_2\text{I}$	44.23	43.90
2,4-diCl	Ab <sup>h</sup>	71	Ethanol	Pale yellow needles	60-61	$\text{C}_7\text{H}_3\text{Cl}_2\text{I}$	44.23	44.08
<i>p</i> -C <sub>2</sub> H <sub>5</sub>	Ab <sup>i</sup>	80	—	Pale yellow oil <sup>j</sup> .	—	$\text{C}_9\text{H}_{11}\text{I}$	51.69	50.91 <sup>k</sup>
<i>o</i> -NO <sub>2</sub>	Ab	75	Ethanol	Yellow plates	73-75 <sup>l</sup>	$\text{C}_7\text{H}_5\text{INO}_2$	48.25	48.12
<i>p</i> -COOH	Aa	69	Ethyl acetate	Pale yellow needles	237-239 <sup>m</sup> dec.	$\text{C}_8\text{H}_7\text{IO}_2$	48.43	48.35
<i>p</i> -CH <sub>3</sub>	B	95.5	Hexane	Pale yellow needles	47-48	$\text{C}_8\text{H}_9\text{I}$	54.68	54.54
<i>m</i> -CH <sub>3</sub>	B <sup>n</sup>	57	—	Straw liquid <sup>k, o</sup>	—	$\text{C}_8\text{H}_9\text{I}$	54.68	<sup>k</sup>
<i>o</i> -CH <sub>3</sub>	B	83	Pet. ether	Almost colorless needles <sup>p</sup>	34-35 <sup>q</sup>	$\text{C}_8\text{H}_9\text{I}$	54.68	54.41
<i>m</i> -NO <sub>2</sub>	B <sup>r</sup>	36	Ethanol	Yellow rods	83.5-85.5 <sup>r</sup>	$\text{C}_7\text{H}_5\text{INO}_2$	48.25	48.48

<sup>a</sup> *p*-Chlorobenzyl chloride (Eastman P-1103), b.p. 103° at 16 mm. <sup>b</sup> Reported m.p. 64° (1). <sup>c</sup> *p*-Bromobenzyl bromide, m.p. 63-64° (2). <sup>d</sup> Reported m.p. 80-81° (3), m.p. 73° (4). <sup>e</sup> *p*-Iodobenzyl bromide, m.p. 78-80° (5). <sup>f</sup> Calculated only for the aliphatic (reactive) iodide in the molecule. <sup>g</sup> 3,4-Dichlorobenzyl chloride (Heyden Chem. Co.), b.p. 99.5-101° at 2 mm. <sup>h</sup> 2,4-Dichlorobenzyl chloride (Heyden Chem. Co.), b.p. 99-101.5° at 3.5 mm. <sup>i</sup> *p*-Ethylbenzyl chloride, b.p. 107-110° at 20 mm. (6). <sup>j</sup> b.p. 100.5-105° at 2.5 mm. <sup>k</sup> Decomposes rapidly in dark to red oil. <sup>l</sup> Reported m.p. 75° (7). <sup>m</sup> m.p. 244-245° dec. in an evacuated tube. <sup>n</sup> *m*-Tolyl carbinol, b.p. 117-119° (20 mm.). <sup>o</sup> b.p. 68° at 0.02 mm. <sup>p</sup> Decomposed to black tar within two months. <sup>q</sup> Reported m.p. 34° (8). <sup>r</sup> *m*-Nitrobenzyl alcohol (9). <sup>s</sup> Reported m.p. 83-84° (10).

column afforded 63.7 g. (58%) of *p*-fluorobenzyl iodide, b.p. 57–58° at 0.08 mm., as a pale yellow liquid which darkened on standing. The product solidified in the refrigerator and then was dissolved in hexane. The hexane solution was extracted with 5% sodium thiosulfate and dried over magnesium sulfate. Upon cooling *p*-fluorobenzyl iodide separated as colorless rods which turned pale yellow on filtration, m.p. 34–35°.

*Anal.* Calc'd for  $C_7H_5FI$ : I, 53.77. Found: I, 53.85.

*p*-Methylbenzyl iodide. *Procedure B.* To 12.2 g. (0.1 mole) of *p*-tolyl carbinol, m.p. 59–60°, prepared by the reduction of *p*-toluic acid with lithium aluminum hydride (12), was added 40 ml. of 57% hydriodic acid (*sp. gr.* 1.70). The flask was stoppered, shaken, and placed in the refrigerator for one hour, during which time pale yellow crystals separated. The solid was filtered, washed with water, and dried *in vacuo* to give 22.6 g. (95.5%) of *p*-methylbenzyl iodide, m.p. 46.5–47.5°. Recrystallization from hexane afforded pale yellow needles, m.p. 47–48°. Reported m.p. 45–46.5° (8).

*Anal.* Calc'd for  $C_8H_9I$ : I, 54.68. Found: I, 54.54.

*o*-Tolylcarbinol. To a suspension of 9.5 g. (0.25 mole) of lithium aluminum hydride in 200 ml. of anhydrous ether was added dropwise over a period of 2¼ hours 27.6 g. (0.2 mole) of *o*-toluic acid in 200 ml. of anhydrous ether. The suspension was stirred and refluxed for an additional ¾ hour, and then hydrolyzed by the cautious addition of water, and finally dilute sulfuric acid. The mixture was extracted with ether, the ether layer extracted twice with dilute sodium carbonate solution and then once with water, and the ether layer was dried over sodium sulfate. After removal of the drying agent and evaporation of the ether, the residual oil was distilled, b.p. 85.5–86.5° at 0.75 mm. There was obtained 17.0 g. (70% yield) of colorless *o*-tolylcarbinol.

*o*-Nitrobenzyl bromide. *o*-Nitrotoluene (68.6 g., 0.5 mole) was mixed with 300 ml. of dry carbon tetrachloride. To this mixture was added 88.5 g. (0.5 mole) of *N*-bromosuccinimide and 0.5 g. of benzoyl peroxide and the mixture was refluxed for 9½ hours. After cooling the succinimide was removed, and the carbon tetrachloride solution was concentrated under reduced pressure. The oily liquid so obtained crystallized in the refrigerator to give 37.6 g. (43% yield) of yellow plates, m.p. 46–47.5°, after one crystallization from ethanol. Reported m.p. 46–47° (13).

*p*-Bromomethylbenzoic acid. To a refluxing solution of 27.2 g. (0.2 mole) of *p*-toluic acid, m.p. 178–180°, in 400 ml. of benzene was added 32 g. (0.2 mole) of bromine over a period of 2½ hours, during which time the reaction mixture was irradiated with a 100-watt clear incandescent bulb. After the addition of half of the bromine a precipitate of *p*-bromomethylbenzoic acid started to separate. The reaction mixture was heated for an additional hour after all of the bromine had been added. After cooling to room temperature, the acid which had crystallized was collected and amounted to 28.6 g. (66.5%) of a light tan solid, m.p. 224–226°. Recrystallization from ethyl acetate afforded colorless plates, m.p. 227.5–229°. Reported m.p. 223° (14).

*1*-Iodomethylnaphthalene. Attempts to prepare this compound from 1-chloromethylnaphthalene (15), b.p. 125° at 0.1 mm., by Procedure A gave a pale yellow solid which decomposed rapidly to a black tar before it could be isolated.

*2*-Iodomethylnaphthalene. This compound was prepared from 15.2 g. (0.069 mole) of 2-bromomethylnaphthalene (16), m.p. 52.5–54°, by Procedure A. The pale yellow solid, m.p. 72–73.5°, thus obtained decomposed rapidly to a black tar and could not be obtained in pure form.

*4*-Iodomethyl-2-phenyl-1,2,3,2*H*-triazole. This compound was prepared from 4.25 g. (0.0243 mole) of 4-hydroxymethyl-2-phenyl-1,2,3,2*H*-triazole, m.p. 65–66°, by Procedure B. The crude product was crystallized from ethanol to give 5.7 g. (83%) of almost colorless lath-shaped crystals, m.p. 72–75°. Recrystallization from ethanol afforded pure 4-iodomethyl-2-phenyl-1,2,3,2*H*-triazole, m.p. 72–74°.

*Anal.* Calc'd for  $C_9H_8IN_3$ : I, 44.51. Found: I, 44.17.

## SUMMARY

Thirteen ring-substituted benzyl iodides have been prepared for use in studying the exchange of benzyl type iodides with radioactive iodide ion. These compounds were prepared by reaction of the corresponding chloride or bromide with sodium iodide in dry acetone or by treatment of the arylcarbinol with concentrated hydriodic acid.

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