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for the Preparation
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Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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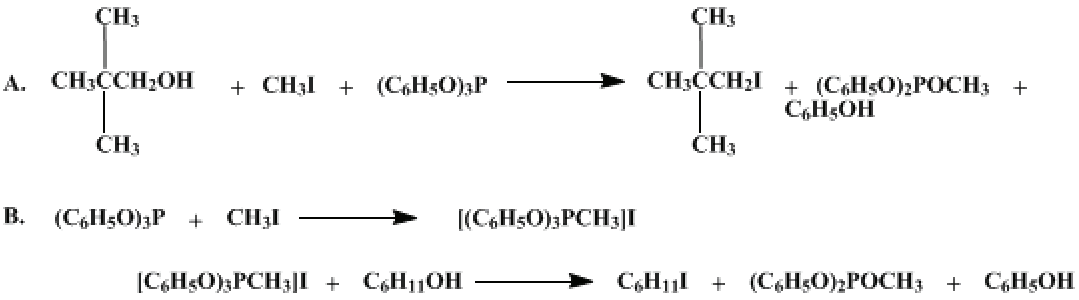
ALKYL IODIDES: NEOPENTYL IODIDE AND IODOCYCLOHEXANE

[Propane, 1-iodo-2,2-dimethyl- and Cyclohexane, iodo-]



$$\text{A.}\quad CH_3\overset{CH_3}{\underset{CH_3}{C}}CH_2OH + CH_3I + (C_6H_5O)_3P \longrightarrow CH_3\overset{CH_3}{\underset{CH_3}{C}}CH_2I + (C_6H_5O)_2POCH_3 + C_6H_5OH$$

$$\text{B.}\quad (C_6H_5O)_3P + CH_3I \longrightarrow [(C_6H_5O)_3PCH_3]I$$

$$[C_6H_5O)_3PCH_3]I + C_6H_{11}OH \longrightarrow C_6H_{11}I + (C_6H_5O)_2POCH_3 + C_6H_5OH$$

Submitted by H. N. Rydon[1]
Checked by W. Fuhrer, R. Keese, and A. Eschenmoser.

1. Procedure

Note. Two procedures are given. Procedure A is the simplest to perform, but B is preferred for sensitive alcohols and in cases where elimination to olefins is expected, for example, with all tertiary and many secondary alcohols. Procedure A is best for sterically hindered alcohols, for example, neopentyl alcohol.

Caution! Methyl iodide, in high concentrations for short periods or in low concentrations for long periods, can cause serious toxic effects in the central nervous system. Accordingly, the American Conference of Governmental Industrial Hygienists[2] has set five p.p.m., a level which cannot be detected by smell, as the highest average concentration in air to which workers should be exposed for long periods. The preparation and use of methyl iodide should always be performed in a well-ventilated fume hood. Since the liquid can be absorbed through the skin, care should be taken to prevent contact.

A. *Neopentyl iodide*. A 500-ml., two-necked, round-bottomed flask fitted with a reflux condenser equipped with a calcium chloride drying tube is charged with 136 g. (115 ml., 0.439 mole) of triphenyl phosphite, 35.2 g. (0.400 mole) of neopentyl alcohol, and 85 g. (37 ml., 0.60 mole) of methyl iodide (Note 1). A thermometer of sufficient length extends into the liquid contents of the flask. The mixture is heated under gentle reflux with an electric heating mantle until the temperature of the refluxing liquid rises from its initial value of 75–80° to about 130°, and the mixture darkens and begins to fume. The time required is about 24 hours. It is necessary to adjust the heat input from the mantle from time to time as the reaction proceeds and the reflux rate diminishes (Note 2).

The reaction mixture is distilled under reduced pressure through a 13-cm. Vigreux column. The fraction boiling below 65° (50 mm.) is collected and washed with 50 ml. of water, then with 50-ml. portions of cold 1 *N* sodium hydroxide until the washings no longer contain phenol (Note 3). The product is washed again with 50 ml. of water, dried over calcium chloride and redistilled, yielding 51–60 g. (64–75%) of neopentyl iodide, b.p. 54–55° (55 mm.), n_D^{21} 1.4882 (Note 4).

B. *Iodocyclohexane*. A 500-ml., two-necked, round-bottomed flask fitted with a reflux condenser equipped with a calcium chloride drying tube is charged with 124 g. (107 ml., 0.400 mole) of triphenyl phosphite and 85 g. (37 ml., 0.60 mole) of methyl iodide (Note 1). A thermometer of sufficient length extends into the liquid contents of the flask. The mixture is heated under gentle reflux with a heating mantle until the internal temperature has risen to about 120°. At this point the mixture is dark and viscous (Note 5). The flask is cooled, and 40 g. (0.40 mole) of cyclohexanol is added to the oily methyltriphenoxyphosphonium iodide. The mixture is shaken gently until homogeneous (Note 6) and allowed to stand overnight at room temperature (Note 7). The mixture is distilled through a 13-cm.

Vigreux column (Note 8), yielding 62.5–63 g. (74–75%) of iodocyclohexane, b.p. 66–68° (12 mm.), n_D^{22} 1.5475.

2. Notes

1. The use of 1.2 instead of 1.5 equivalents of methyl iodide proved beneficial in some runs carried out by the checkers; some difficulty was experienced in reaching the recommended final temperature.
2. To obtain the yields cited, it is essential that the reaction temperature reaches the indicated, final value, but heating should not be unnecessarily prolonged. The reaction is conveniently monitored by IR spectroscopy. As the reaction proceeds, a broad, strong band at 865 cm.$^{-1}$ with a shoulder at 880 cm.$^{-1}$ disappears, and another broad, strong band at 945 cm.$^{-1}$ and a sharp, medium band at 1310 cm.$^{-1}$ appear.
3. Testing with iron(III) chloride is recommended.
4. The product contains about 5% of *tert*-amyl iodide (^{1}H NMR); this is in agreement with the finding of Kornblum and Iffland,[3] who describe a simple way of removing this impurity.
5. As in procedure A, the heat input should be increased from time to time, and it is essential to attain the recommended final temperature; unnecessarily prolonged heating after this is reached should be avoided as the phosphonium iodide decomposes at high temperatures.
6. With some alcohols (*e.g.*, cyclohexanol) there is no appreciable rise in temperature, with others (*e.g.*, *tert*-amyl alcohol) it may be considerable, in which case the mixture should be cooled with water. In addition, there may be an induction period of up to 1 hour.
7. The reaction may be followed by IR spectroscopy: a strong, broad band at 1040 cm.$^{-1}$ disappears, and a similar band appears at 945 cm.$^{-1}$. The reaction appears to be complete after 6 hours.
8. It is not necessary to remove phenol from the reaction mixture if the alkyl iodide has a boiling point well below that of phenol. For isolation of higher boiling alkyl iodides phenol should be removed by dissolving the reaction mixture in ether (400 ml.) and washing as in procedure A.

3. Discussion

The methods described above are applicable to almost any alcohol. Procedure A is best for sterically hindered alcohols, while procedure B is especially useful for alcohols sensitive to rearrangement or alkene formation. The submitter's results for the conversion of a number of alcohols to the iodides on a preparative scale are summarized in Table I.

TABLE I
IODIDES FROM ALCOHOLS

Iodide	Procedure	Yield, %	Boiling Point, °C.
n-Butyl iodide	A	80	126–128° (760 mm.)
n-Hexyl iodide	A	75	64–66° (15 mm.)
2-Phenylethyl iodide	A	95	94–95° (1.5 mm.)
1,3-Diiodo-2,2-dimethylpropane[a]	A	75	70–71° (0.1 mm.)
tert-Amyl iodide	B	80	50–52° (50 mm.)
Ethyl 3-iodopropionate	B	90	65–66° (8 mm.)

[a] Reference 4.

Landauer and Rydon[4] describe the application of the method, on a smaller scale, to numerous other iodides; they also prepared alkyl bromides and alkyl chlorides by substituting benzyl bromide and benzyl chloride, respectively, for methyl iodide.

The preparation of alkyl iodides by the phosphorus and iodine method is described in an earlier volume of *Organic Syntheses*.[56]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 634

References and Notes

1. Department of Chemistry, The University, Exeter EX4 4QD, England.
2. American Conference of Governmental Industrial Hygienists (ACGIH), "Documentation of Threshold Limit Values," 3rd ed., Cincinnati, Ohio, 1971, p. 166.
3. N. Kornblum and D. C. Iffland, *J. Am. Chem. Soc.*, **77**, 6653 (1955).
4. S. R. Landauer and H. N. Rydon, *J. Chem. Soc.*, 2224 (1953).
5. W. W. Hartman, J. R. Byers, and J. B. Dickey, *Org. Synth.*, **Coll. Vol. 2**, 322 (1943); H. S. King, *Org. Synth.*, **Coll. Vol. 2**, 399 (1943).
6. A. Campbell and H. N. Rydon, *J. Chem. Soc.*, 3002 (1953).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

calcium chloride (10043-52-4)

ether (60-29-7)

sodium hydroxide (1310-73-2)

Cyclohexanol (108-93-0)

phenol (108-95-2)

benzyl chloride (100-44-7)

iron(III) chloride (7705-08-0)

Methyl iodide (74-88-4)

iodide (20461-54-5)

tert-amyl alcohol (75-85-4)

benzyl bromide (100-39-0)

2-Phenylethyl iodide (17376-04-4)

Iodocyclohexane,
Cyclohexane, iodo- (626-62-0)

Ethyl 3-iodopropionate (6414-69-3)

Neopentyl alcohol (75-84-3)

Neopentyl iodide,
Propane, 1-iodo-2,2-dimethyl- (15501-33-4)

triphenyl phosphite (101-02-0)

methyltriphenoxyphosphonium iodide (17579-99-6)

phosphonium iodide (12125-09-6)

n-Butyl iodide (542-69-8)

tert-amyl iodide (594-38-7)

n-Hexyl iodide (638-45-9)