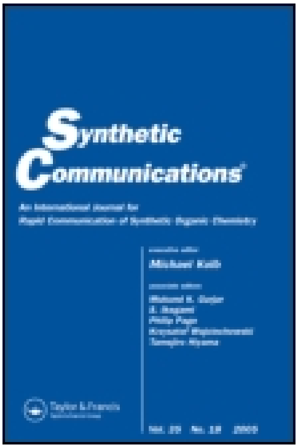


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

NEW HALOGENATION REAGENT SYSTEM FOR ONE-POT CONVERSION OF ALCOHOLS INTO IODIDES AND AZIDES*

Ahmed Kamal [a], G. Ramesh [a] & N. Laxman [a]
[a] Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

To cite this article: Ahmed Kamal, G. Ramesh & N. Laxman (2001): NEW HALOGENATION REAGENT SYSTEM FOR ONE-POT CONVERSION OF ALCOHOLS INTO IODIDES AND AZIDES*, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:6, 827-833

To link to this article: http://dx.doi.org/10.1081/SCC-100103316

SYNTHETIC COMMUNICATIONS, 31(6), 827–833 (2001)

NEW HALOGENATION REAGENT SYSTEM FOR ONE-POT CONVERSION OF ALCOHOLS INTO IODIDES AND AZIDES*

Ahmed Kamal,[†] **G. Ramesh, and N. Laxman**

Division of Organic Chemistry, Indian Institute of
Chemical Technology, Hyderabad 500 007, India

ABSTRACT

In situ generation of hydrogen iodide from methanesulphonic acid/sodium iodide in different solvents was found to be an attractive reagent system for the chemoselective conversion of various alcohols to their corresponding iodides. Moreover, treatment of benzylic and allylic alcohols with this reagent system, followed by substitution with azide ion, produced the corresponding azides in one pot in good yields.

Alkyl halides, especially iodides, have been useful for the ionic or radical carbon-carbon coupling reaction. In various synthetic organic reactions, such as substitution, elimination, and rearrangements, they are intermediates of choice. The earlier developed methods for the conversion of alcohols into iodides have employed phosphorous-based reagents.[1–3] These reagents have now been replaced by triphenylphospine in combination with a halogen source such as N-iodosuccinamide[4] or triiodoimidazole.[5–7]

---

* IICT Communication No. 4529.

[†] Corresponding author.

All these reactions usually require elevated temperatures and long reaction times. Recently, trimethylsilyl chloride or boron trifluoride etherate with sodium iodide has been used for the conversion of allylic alcohols into allylic iodides.[8,9] However, the activation reagents for such procedures are expensive and not very easy to handle. A major difficulty experienced with phosphite-based reagent systems is that the triphenylphosphine and its oxides are difficult to remove from the reaction mixture. They are removed either by precipitation or chromatography, which is cumbersome and results in reduced yields. Therefore, this method is particularly inconvenient in large-scale synthesis. Some of the many existing methods for the conversion of alcohols to iodides[10–12] are generally not selective, therefore a search for more facile and practical methods that could employ inexpensive reagents for the chemoselective iodination/azidation is worthwhile.

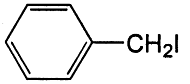
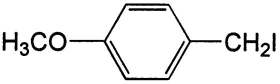
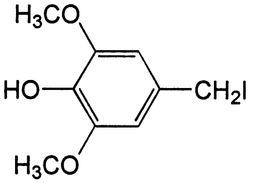
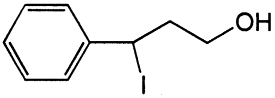
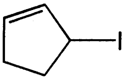
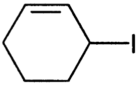
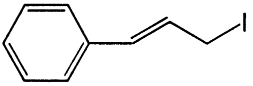
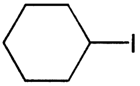
In our recent studies on the synthesis of some new analogs of natural products, we were confronted with the challenge of employing a selective and useful method for the conversion of benzylic/allylic alcohols to their corresponding iodides without affecting the other susceptible functionalities. In this endeavour, it was envisaged that organic sulphonic acids and sodium iodide could offer an immediate source of hydrogen iodide. Herein, we report methanesulphonic acid-sodium iodide as an efficient reagent system for the conversion of alcohols to iodides. This reagent system has not been much explored in organic synthesis except for the reduction of sulphoxides to the corresponding sulphides.[13]

$$\underset{\textbf{1a - l}}{\text{R-OH}} \xrightarrow[\text{CH}_3\text{CN or Cl(CH}_2)_2\text{Cl}]{\text{CH}_3\text{SO}_3\text{H/NaI}} \underset{\textbf{2a - l}}{\text{R-I}}$$

R = alkyl, benzyl, allyl

In the present work, alkyl, allyl, and benzylic alcohols have been converted to their corresponding iodides in good to excellent yields employing methanesulphonic acid and sodium iodide reagent system. The iodination for benzylic, allylic, and tertiary alcohols has been performed by this reagent system generally employing acetonitrile as the solvent. These conversions take place with spontaneity (10–20 m) in excellent yields at room temperature as described[14] in Table 1 (**1a**–**1h**). Other solvents, such as dichloromethane, dichloroethane, and toluene, have also been examined, but no significant improvement has been observed. Primary and secondary alcohols (**1i**–**1l**) also give the corresponding iodides by employing dichloroethane as a solvent under reflux conditions. Whereas, it has been observed that primary and secondary alcohols do not produce their iodo derivatives at

Table 1. Iodination of Alcohols by Methanesulphonic Acid-Sodium Iodide Reagent System **2a–l**

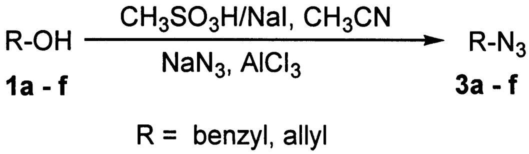
Entry	Product[b]	Time	Yield (%)
1a		15 min	92
1b		15 min	90
1c		15 min	88
1d		15 min	88
1e		20 min	75
1f		20 min	80
1g		20 min	85
1h	$(C_2H_5)_3C\text{-}I$	10 min	89
1i[a]		26 h	65
1j[a]	$CH_3(CH_2)_4CH_2I$	8 h	71
1k[a]	$CH_3(CH_2)_6CH_2I$	8 h	70
1l[a]	$CH_3(CH_2)_9CH_2I$	8 h	71

[a] The reactions for these alcohols have been carried out in dicholormethane at reflux temperature.

[b] All the products have shown satisfactory spectral data.

room temperature. The chemoselectivity by this reagent system has been illustrated in the case of **1d**, wherein the benzylic group alone has been converted to its iodo form **2d**. Therefore, this reagent system could be used for the selective iodination of benzylic, allylic, and tertiary alcohols without converting the primary and secondary alcohols at room temperature. Further, when these reactions were carried out in acetonitrile, the conversions took longer reaction times (24–48 h).

The present investigation has also been extended towards the azidation of benzylic and allylic alcohols in acetonitrile with catalytic amount of aluminium chloride in one pot. It has been observed that the azidation[15] of allylic alcohols (**1e**, **f**) is very facile and takes place at room temperature. However, the azidation of benzyl alcohols (**1a**, **b**, **c**, and **d**) require reflux conditions. Similar to selective iodination, the azidation in case of **1d** takes place in a selective manner for the benzylic alcoholic group.



$$\underset{\mathbf{1a-f}}{\text{R-OH}} \xrightarrow[\text{NaN}_3,\ \text{AlCl}_3]{\text{CH}_3\text{SO}_3\text{H/NaI},\ \text{CH}_3\text{CN}} \underset{\mathbf{3a-f}}{\text{R-N}_3}$$

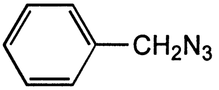
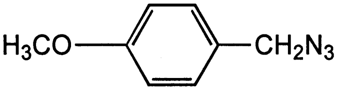
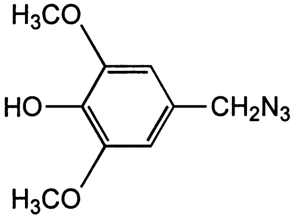
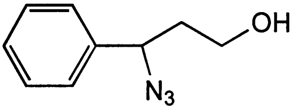
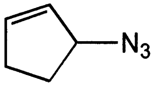
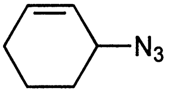
R = benzyl, allyl

In conclusion, we have described an efficient, chemoselective, and practical procedure for the conversion of various alcohols to their iodides, which will have wide application in organic synthesis because of its simplicity and chemoselectivity. Furthermore, the treatment of allylic and benzylic alcohols by this reagent system described also offers a convenient method for the preparation of corresponding azides, which are valuable starting materials in organic synthesis. The same strategy has a potential for the preparation of a wide variety of benzylic and allylic compounds. The extension and further applications of this method are now in progress in our laboratory.

EXPERIMENTAL

IR spectra were recorded on a IR Nicolet 740 FT IR spectrometer. ^{1}H NMR spectra were recorded on a FT (200 MHz Gemini) spectrometer. Mass spectra were recorded on either a Micromass 7070h or Finnigan Mat 1020 B mass spectrometer operating at 70 eV. Thin-layer chromotography was done on precoated silica gel 60f 254 (0.5 mm) glass plates. All the alcohols were purchased from a local company and used directly as received.

Table 2. Azidation of Benzylic and Allylic Alcohols

Entry	Product[a]	Yield (%)
1a		65
1b		63
1c		60
1d		58
1e		50
1f		57

[a]All the products gave satisfactory spectral data.

All reagents were obtained from commercial suppliers and were used without further purification.

Note: All the compounds are fully characterized by ^{1}H NMR and IR spectroscopy and compared with authentic samples.

General Procedure for 2a–h

To a vigorously stirred solution of NaI (596 mg, 4 mmol) and benzyl alcohol (216 mg, 2 mmol) in acetonitrile (10 mL) under nitrogen is added methanesulphonic acid (384 mg, 4 mmol) in 2 mL of acetonitrile with a syringe at room temperature. The reaction mixture was allowed to stir for 15 m quenched with water, and extracted with ether (20 mL). The organic layer was washed with 10% sodium thiosulphate solution and dried over anhydrous sodium sulphate. Upon evaporation, crude iodide was obtained. This was purified by column chromatography on silica gel by eluting with hexane, giving the benzyl iodide in 92% yield.

General Procedure 3

To a vigorously stirred solution of NaI (596 mg, 4 mmol) and benzyl alcohol (216 mg, 2 mmol) in acetonitrile (10 mL) under nitrogen was added methanesulphonic acid (384 mg, 4 mmol) in 2 mL of acetonitrile with a syringe at room temperature. The reaction mixture was allowed to stir for 15 m, to which was added anhydrous aluminum chloride (26 mg, 0.2 mmol) and sodium azide (390 mg, 6 mmol), and refluxed for 5 h. The reaction mixture was then quenched with water and extracted with ether (20 mL). The organic layer was washed with 10% sodium thiosulphate solution and dried over anhydrous sodium sulphate. Upon evaporation, crude azide was obtained. This was purified by column chromatography on silica gel by eluting with hexane, giving the benzyl azide in 65% yield.

ACKNOWLEDGMENTS

NL is thankful to CSIR (New Delhi) for the award of a Senior Research Fellowship.

REFERENCES

1. Landauer, S.R.; Rydon, H.N. J. Chem. Soc. **1953**, 2224.
2. Coe, D.G.; Landauer, S.R.; Rydon, H.N. J. Chem. Soc. **1954**, 2281.
3. Rydon, H.N.; Tonge, B.L. J. Chem. Soc. **1956**, 3043.
4. Hanessian, S.; Ponpipom, M.M.; Lavallee, P. Carbohydr. Res. **1972**, *24*, 45.
5. Garegg, P.J.; Samuelsson, B. J. Chem. Soc. Perkin Trans. 1 **1980**, 2866.
6. Classon, B.; Garegg, P.J.; Samuelsson, B. Can. J. Chem. **1981**, *59*, 339.
7. Garegg, P.J.; Johansson, R.; Ortega, C.; Samuelsson, B. J. Chem. Soc. Perkin Trans. 1 **1982**, 681.
8. Kanai, T.; Irifune, S.; Ishii, Y.; Ogawa, M. Synthesis **1989**, 283.
9. Vankar, Y.D.; Kavita, S. Tetrahedron Lett. **1991**, *32*, 1081.

10. Buehler, C.A.; Person, D.E. Survey of Organic Chemistry; Wiley Interscience: New York, 1977; Vol. II.
11. Olah, G.A.; Narang, S.C.; Gupta, B.G.B.; Malhotra, R. J. Org. Chem. **1979**, *44*, 1247.
12. Morita, T.; Yoshida, S.; Okamoto, Y.; Sakurai, H. Synthesis **1979**, 379.
13. Drabowicz, J.; Dudzinski, B.; Mikolajczyk, M. Synlett **1992**, 252.

Received in Japan March 27, 2000