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Research Article

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Sodium iodide as a novel, chemoselective and highly efficient catalyst for *N*-tert-butoxy Carbonylation of amines at room temperature.

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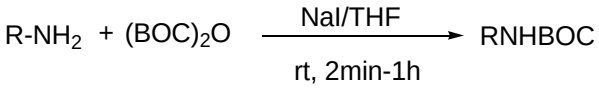
ABSTRACT

Commercially available sodium iodide was found to be one of the best catalyst and practically an efficient protocol for the protection of various structurally and electronically divergent aryl and aliphatic amines using $(BOC)_2O$ at room temperature is presented. The reported method is chemo selective and the products isolated in high yields.

Keywords: Sodium iodide, Boc anhydride, Chemo selective, Aryl and Aliphatic amines.

INTRODUCTION

Scheme1.Sodium iodide catalyzed *N*-BOC protection of Amines.



In synthetic organic/medicinal chemistry, the presence of the amine functionality in a wide range of molecules makes the protection of amines continues to be an important technique [1].The most widely used BOC anhydride for the protection of structurally divergent amines is well known in the literature.

Because of its resistant to nucleophilic reagents, strong basic conditions and racemization during peptide synthesis makes the BOC group as frequently used technique in organic synthesis [2]. Different kinds of reagents and techniques have been developed for introducing the BOC group and the most reactions are carried out in the presence of a base such as DMAP [3]/inorganic bases [4]. And also with (i) tert-butyl-1-chloroalkyl carbonates in the presence of K_2CO_3 in H_2O-THF[1a] (ii) 1-tert-butoxy-2-tert-butoxy Carbonyl-1,2 dihydroisoquinoline(BBDI) in hexane/benzene[5] (iii) coper(II) tetrafluroborate/solvent free conditions[6] (iv) molecular iodine(10 mol%)/solvent free[7] (v) yttria-zirconia in MeCN[8] (vi) $Zn(ClO_4)_2$.$6H_2O$ in DCM[9] (vii) $ZrCl_4$ in MeCN[10]. And the more recent methods including (viii) Pyridinium-2,2,2-trifluoroacetate ionic liquid [11] (ix) Amberlyst RA 21 solid base resin as a reusable heterogeneous catalyst[12] (x) N-sulfonic acid poly(4-vinylpyridinium) chloride as a reusable solid acid catalyst[13] (xi)1,3-disulfonic acid imidazolium hydrogen sulphate as a reusable ionic liquid catalyst[14] (xii) Zinc catalyst[15](xiii)1-alkyl-3-methylimidazoliumcation[16] (xiv) Ferric chloride[17] (xv)1,1,1,3,3,3-hexafluoroisopropanol a recyclable organic catalyst[18] (xvi) Bromodimethylsulfonium bromide[19] (xvii)Sulfonic acid functionalized silica[20]

All of the above literatures reported different methodology for the protection of amines & are of good interest to know but it has had the following disadvantages:
1. At least one or two steps are added as an increment for the protection of amines and before initiating the reaction, time is consumed for the preparation of the reagent/catalyst.

2. Costly reagents/catalysts which is limited for industrial application.
3. Highly toxic, hazardous, long reaction times, low yields and adverse reaction that produce a mixture of products and multiple stages including purification of the corresponding protected amines.
4. The presence of electron donating and withdrawing groups impacts on their yield.
5. Various side reactions are associated with base catalyzed reactions such as the formation of urea, bicarboamoylation and isocynates.

The present methodology describes the use of sodium iodide is an efficient catalyst and protocol for the protection of amines which provided the corresponding N-tert-butyloxy of the amines in excellent yield.

EXPERIMENTAL SECTION

General Considerations:
All reagents and catalyst purchased from commercial sources were used as received. All melting points are uncorrected. The ^{1}H and ^{13}C NMR spectra are referenced to the residual

Solvent signals (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C in $CDCl_3$). All reactions were carried out in oven-dried glassware and were magnetically stirred.

General procedure: To a magnetically stirred mixture of amine (1equiv), sodium iodide(1.0equiv) in Tetrahydrofuran and $(BOC)_2O$ (1.2 equiv) was added dropwise and the reaction mixture was stirred at room temperature for the specified time (Table 1). Ethylacetate (20ml) was added. The reaction mixture was washed with $Na_2S_2O_3$ (5%, 15ml) and the saturated $NaHCO_3$ and dried overNa_2SO_4, the solvent was evaporated under reduced pressure and the residue was purified by triturating with 10% (n-hexane: EtoAC) mixture, gave the corresponding pure product.

Tert-Butyl Isopropyl Carbamate (Entry 1, Table-1):
Melting point: 72-78^{0}C.
IR(Nacl)cm^{-1}:1681.98.^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.12(d,6H,*J*=6.3Hz,2CH_3),1.44(s,9H,*t*-butyl),3.81-3.69(m, 1H, CH), 4.41(brS, 1H,NH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 23.09,28.14,28.42.52,78.92,155.18.

Tert-Butyl Di n-propyl Carbamate (Entry 2, Table-1):
IR(Nacl)cm^{-1}:1691.63.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H0.86(t,3H,*J*=7.5Hz,2CH_3),1.45(s,9H,*t*-butyl), q,4H,*J*=7.5Hz,2CH_2),3.12(s,4H,2NCH_2).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 11.26,21.47,21.92,28.44,48.76,78.85,155.74.

1-Tert-Butyl 4-Ethyl Piperdine-1,4-diCarboxylate (Entry 3, Table-1):
IR(Nacl)cm^{-1}:1732.13,1693.56.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.25(t,3H,*J*=7.2Hz, CH_3), 1.45(s,9H,*t*-butyl), 1.68-1.52(m, 4H, 2CH_2), 1.85(dd, 2H, *J*=13.5Hz, *J*=2.4Hz,CH_2), 2.48-2.38(m,1H,CH),2.83(t,2H,*J*=11.4Hz,CH_2),4.14(q,2H,*J*=7.2Hz,CH_2).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C14.19,27.40,27.96,28.41,29.67,41.14,43.08,60.47,79.53,154.70,174.59.

Tert-Butyl 4-methyl piperazine-1-carboxylate (Entry 4, Table-1):
IR(Nacl)cm^{-1}:1698.38.
^{1}HNMR(300MHZ, $CDCl_3$): δ_H1.46(s, 9H, *t*-butyl), 2.30(s, 3H, CH_3),2.34(t,4H, *J*=4.8Hz,2CH_2),3.44(t, 4H,*J*=4.8Hz, 2CH_2).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.40,46.19,54.81,79.58,154.72.

Tert-Butyl morpholine-4-carboxylate (Entry 5, Table-1):
Melting point:70-75^{0}C. IR(Nacl)cm^{-1}:1693.56.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.46(s,9H,*t*-butyl),3.41(t,4H,*J*=4.5Hz,2CH_2),3.64(t,4H,*J*=4.5Hz,2CH_2).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.36,66.64,79.90,154.75.
Anal.Calcd for $C_9H_{17}NO_3$: C,57.73;H,9.15;N,7.48.Found:C,58.04;H,9.13;N,7.97.

Tert-Butyl cyclopropyl methyl carbamate (Entry 6, Table-1):
IR(Nacl)cm^{-1}:1693.56.
^{1}HNMR(300MHZ,$CDCl_3$):
δ_H0.17(q,2H,*J*=5.1Hz,CH_2),0.46(q, 2H, *J*=5.1Hz,CH_2), 1.00-0.87(m,1H,CH),1.44(s,9H,*t*-butyl),2.98(t,2H,*J*=6.0Hz, NCH_2), 4.69(brS,1H,NH).

^{13}CNMR(300MHZ,$CDCl_3$):δ_C3.16,11.01,11.59,27.39,28.40,45.43,79.03,155.86.
Tert-Butyl-1,3-dioxohexahydro-1H-isoindole-2(3H)-carboxylate (Entry 7, Table-1):
Melting point:112-117^{0}C. IR(Nacl)cm^{-1}:1813.15,1757.21,1712.85.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.45(s, 9H, *t*-butyl),1.70-1.61(m, 2H, CH_2), 1.91(dd, 2H, *J*=13.5, 3.0Hz, CH_2), 2.53-2.44 (m, 2H,CH), 2.85(t,2H,*J*=11.4Hz,CH_2),4.02(d,2H,*J*=10.2Hz).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 27.72,28.42,40.82,43.00,79.80,154.77,180.26.
Anal.Calcd for $C_{13}H_{19}NO_4$: C,61.64;H,7.56;N,5.53.Found:C,61.68;H,7.52;N,5.32.

Tert-Butyl-1,3-dioxo-1,3,3a,4,7,7a-tetrahydro-1H-isoindole-2(3H)-yl-carbamate(Entry 8, Table-1):
Melting point: 100-108^{0}C. IR(KBr)cm^{-1}:1800.61,1756.52,1713.81.
^{1}HNMR(300MHZ,$CDCl_3$:δ_H1.56(s,9H,*t*-butyl),2.31-2.23(m,2H,CH_2),2.63-2.57(m,2H,CH),3.18-3.10(m, 2H, CH_2), 5.98-5.90(m,2H,olefinic-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C27.72,28.42,40.82,43.00,79.80,154.77,180.26.
Anal.Calcd for $C_{13}H_{17}NO_4$: C,62.14;H,6.82;N,5.57.Found:C,62.15;H,7.02;N,5.45.

Di tert-Butyl piperazine-1,4-dicarboxylate (Entry 9, Table-1):
Melting point: 155-163^{0}C. IR(Nacl)cm^{-1}:1691.63.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H 1.47(s,18H,*t*-butyl),3.39(s,8H,CH_2).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.38,28.64,43.53,80.01,154.68.

Tert-Butyl Phenyl Carbamate (Entry 10, Table-1):
Melting point:132^{0}C. IR(KBr)cm^{-1}: 1689.70.
^{1}HNMR(300MHZ,CDCl3):δ_H 1.54(s,9H,*t*-butyl), 6.49(brS,1H,NH), 7.05-7.00(m,1H,Ar-H),7.29(d,2H, *J*=7.2 Hz, Ar-H),7.35(d,2H,*J*=7.8 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 28.35,80.50,118.55,123.03,128.97,138.34,152.76.

Tert-Butyl 4-fluorophenyl carbamate (Entry 11, Table-1):
IR(KBr)cm^{-1}:1695.49.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H 1.51(s, 9H, *t*-butyl), 6.46(brS, 1H, NH), 7.00-6.93(m, 2H, Ar-H),7.30(dd, 2H, *J*=8.7Hz, *J*=8.4Hz,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.33,80.64,115.40,115.70,120.35,134.28,134.31,152.90,157.16,160.36.

Tert-Butyl-2-methylphenyl carbamate (Entry 12, Table-1):
Melting point: 75-80^{0}C. IR(KBr)cm^{-1}:1691.93.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H 1.52(s, 9H, t-butyl), 2.24(s, 3H, CH_3), 6.28(brS, 1H, NH), 7.01-6.95(m, 1H, Ar-H),7.21-7.12(m, 2H, Ar-H), 7.79(d,1H, *J*=7.8 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 17.73,28.36,80.42,120.91,123.65,126.80,130.32,136.32,153.08.

Tert-Butyl-4-methylphenyl carbamate (Entry 13, Table-1):
Melting point: 80-85^{0}C. IR(KBr)cm^{-1}:1685.84.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H1.51(s, 9H, *t*-butyl), 2.29(s, 3H, CH_3), 6.44(brS, 1H, NH),7.08(d, 2H, *J*=8.4 Hz, ,Ar-H),7.23(d,2H,*J*=8.4 Hz, ,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C20.73,28.37,80.32,118.69,129.46,132.54,135.74,152.92.

Tert-Butyl-2,5-dimethyl phenyl carbamate (Entry 14, Table-1):
Melting point: 110-115^{0}C. IR(KBr)cm^{-1}:1695.49.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H 1.52(s, 9H, *t*-butyl), 2.19(s, 3H, CH_3), 2.31(s, 3H, CH_3), 6.23(brS, 1H, NH), 6.80(d, 1H, *J*=7.8 Hz, Ar-H),7.01(d,1H,*J*=7.8 Hz, Ar-H), 7.66(s,1H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 17.28,21.24,28.34,80.35,121.21,123.87,124.29,130.10,136.09,136.56,153.07.

Tert-Butyl-4-ethyl phenyl carbamate (Entry 15, Table-1):
Melting point: 80-85^{0}C. IR(KBr)cm^{-1}:1689.70.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.19(t, 3H, *J*=7.5Hz, CH_3), 1.52(s, 9H, *t*-butyl), 2.58(q, 2H, *J*=7.5 Hz, CH_2), 6.48(brS, 1H,NH),7.10(d,2H,*J*=8.4 Hz, Ar-H), 7.26(d,2H,*J*=8.4 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 15.74,27.42,28.20,28.37,80.30,118.80,128.29,135.94,139.06,152.96.

Tert-Butyl Benzyl carbamate (Entry 16, Table-1):
IR(KBr)cm^{-1}:1680.05.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H 1.45(s,9H,*t*-butyl),4.2(s,2H,CH_2),4.90(brS,1H,NH), 7.35-7.22(m,5H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.41,44.67,79.45,127.30,127.46,128.58,138.93,155.90.

Tert-Butyl 4-methoxy phenyl carbamate (Entry 17, Table-1):
IR(KBr)cm^{-1}:1693.56.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H1.50(s,9H,t-butyl),3.76(s,3H,CH_3),6.47(brS,1H,NH), 6.82(dd,2H, *J*=6.6 Hz, Ar-H),7.27(d,2H, *J*=8.7 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$: δ_C 28.38,55.50,80.22,114.17,120.61,131.46,153.23,155.66.

Tert-Butyl 2-(4-methoxyphenyl)ethylcarbamate (Entry 18, Table-1):
IR(KBr)cm^{-1}:1683.91.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.43(s,9H,*t*-butyl),2.73(t,2H,*J*=6.9Hz,CH_2),3.32(t,2H,*J*=6.9Hz,CH_2),3.79(s,3H,OCH_3), 4.54(brS,1H,NH),6.81(d,2H,*J*=8.7 Hz, Ar-H),7.10(d,2H,*J*=8.4 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.42,35.28,41.99,55.27,79.18,113.99,129.73,131.00,155.88,158.21.

Tert-Butyl 4-chloro phenyl carbamate (Entry 19, Table-1):
Melting Point: 95-101^{0}C. IR(KBr)cm^{-1}:1695.49.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.51(s,9H,*t*-butyl),6.51(brS,1H,NH),7.32-7.22(m,4H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.31,80.87,119.71,127.94,128.95,136.95,152.58.

Tert-Butyl 2-phenyl hydrazine carbamate (Entry 20, Table-1):
Melting point: 80-85^{0}C. IR(KBr)cm^{-1}:1699.34.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H 1.49(s,9H,*t*-butyl),5.77(brS,1H,NH),6.44(brS,1H,NH), 6.90-6.80(m,3H,Ar-H),7.25-7.20(m,2H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 28.26,81.23,112.98,120.80,129.16,148.38,156.24.

Tert-Butyl 1-Naphthyl carbamate (Entry 21, Table-1):
Melting point: 93-98^{0}C. IR(KBr)cm^{-1}:1697.41.
^{1}HNMR(300MHZ,$CDCl_3$): δ_H 1.53(s,9H,*t*-butyl),6.87(brS,1H,NH), 7.53-7.42(m,3H,Ar-H),7.61(d,1H, *J*=8.4Hz,Ar-H),7.90-7.81(m,3H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C28.40, 80.69, 118.67, 120.47, 124.48, 125.86, 125.88, 126.03, 126.51, 128.74, 132.96, 134.09,153.55.

Tert-Butyl 1,1'-Bi phenyl4-yl carbamate (Entry 22, Table-1):
IR(KBr)cm^{-1}:1703.20.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.53(s,9H,*t*-butyl),6.54(brS,1H,NH),7.33-7.28(m,1H,Ar-H),7.44-7.39(m,4H,Ar-H),7.57-7.51(m,4H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C28.37,80.66,118.82,126.78,126.93,127.63,128.75,135.95,137.67,140.65,152.75
Tert-Butyl-4-(2,3dichlorophenyl)Piperazine-1-carboxylate (Entry 23, Table-1):
Melting point: 90-95^{0}C. IR(KBr)cm^{-1}:1681.98.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.48(s, 9H, *t*-butyl), 2.98(t, 4H, *J*=4.8Hz, 2CH_2), 3.60(t, 4H,*J*=4.8Hz,2CH_2), 6.92(dd, 1H, *J*=7.2, 2.4 Hz, Ar-H),7.21-7.12(m,2H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.44,51.33,79.89,118.71,124.95,127.49,127.73,134.14,151.06,154.83.
Anal.Calcd for $C_{15}H_{20}Cl_2N_2O_2$:C,54.39;H,6.09;Cl,21.41;N,8.46. Found: C,54.37;H,5.98;Cl,22.35;N,8.30.

Tert-Butyl methyl(phenyl) carbamate (Entry 24, Table-1):
IR(KBr)cm^{-1}:1695.49.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.43(s,9H,*t*-butyl),2.84(s,3H,NCH_3),4.42(s,2H,CH_2), 7.35-7.23(m,5H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C28.46,33.90,52.63,79.67,127.19,127.66,128.23,128.52,129.00,129.74,138.07, 155.88.

Tert-Butyl 1,3-thiazol-2-yl-carbamate (Entry 25, Table-1):
IR(KBr)cm^{-1}:1718.63.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.59(s,9H,t-butyl),6.88(d,1H,*J*=3.6Hz,Ar-H), 7.39(d,1H,*J*=3.6 Hz, Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 28.33,81.80,111.97,136.72,153.09,162.07.

Tert-Butyl 1H-imidazole-1-carboxylate (Entry 26, Table-1):
Melting point: 90-95^{0}C. IR(KBr)cm^{-1}:1756.25.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H 1.63(s,9H,*t*-butyl),7.04(d,1H,*J*=0.6Hz,Ar-H),7.38(d,1H,*J*=1.5Hz,Ar-H),8.08(s,1H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 27.86,28.11,85.55,117.08,130.22,137.04,147.09.

Tert-Butyl-5-methyl Pyridin-2-yl-Carbamate (Entry 27, Table-1):

IR(KBr)cm^{-1}:1682.95.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H2.26(s,9H,*t*-butyl),3.11(s,3H,CH_3),7.45(dd,2H,*J*=8.1,1.8Hz,Ar-H),8.08(s,1H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$):δ_C 22.44,82.36,117.29,131.63,143.58,151.57,155.50,157.62.

Tert-Butyl-1,3-Benzothiazol-6-yl-Carbamate (Entry 28, Table-1):
IR(KBr)cm^{-1}:1718.63.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.54(s, 9H, *t*-butyl), 6.80(brS, 1H, NH), 7.23(dd, 1H, *J*=8.7, 2.1Hz, Ar-H), 8.00(d, 1H, *J*=8.7Hz,Ar-H),8.34(s,1H,Ar-H),8.87(s,1H,NH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.34,80.99,110.68,118.07,123.52,134.99,136.28,149.21,152.69,152.72.

Tert-Butyl-2-[4-(aminosulfonyl)phenyl]ethyl Carbamate (Entry 29, Table-1):
Melting point: 176-180^{0}C. IR(KBr)cm^{-1}: 3389.04,2983.98,1658.84,1531.53.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.35(s,9H,*t*-butyl),2.75(t,2H,*J*=6.9Hz,CH_2),3.14(t,2H,*J*=6.9Hz,CH_2),6.54(brS,1H,NH), 7.30(s,2H,SO_2NH_2),7.37(d,2H,*J*=8.1Hz,Ar-H),7.73(d,2H,*J*=8.1Hz,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$: δ_C 28.19,35.07,41.04,77.59,125.60,129.07,141.91,143.65,155.51.
Anal.Calcd for $C_{13}H_{20}N_2O_4S$:C,51.98;H,6.71;N,9.33;S,10.68. Found:C,51.43;H,6.52;N,9.21;S,12.55.

Tert-Butyl-(1S)-1-Phenylethyl Carbamate (Entry 30, Table-1):
IR(KBr)cm^{-1}:1685.84.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.42(s,9H,*t*-butyl),1.45(s,3H,CH_3),4.80(brS,2H), 7.35-7.22(m,5H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 22.69,28.39,50.19,79.44,125.88,127.12,128.56,144.08,155.10.

Tert-Butyl-(1R)-1-Phenylethyl Carbamate (Entry 31, Table-1):
IR(KBr)cm^{-1}:1685.84.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.42(s,9H,*t*-butyl),1.46(s,3H,CH_3),4.81(brS,2H), 7.35-7.21(m,5H,Ar-H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C22.69,28.39,50.19,79.44,125.88,127.11,128.56,144.07,155.11.

Tert-Butyl-2-(hydroxymethyl)-4-methylpentyl Carbamate (Entry 32, Table-1):
Melting point: 52-58^{0}C. IR(KBr)cm^{-1}:1688.73.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H0.84(d,6H,*J*=2.1Hz,2CH_3),1.12-0.96(m,2H),1.41(s,9H,*t*-butyl),1.65-1.54(m,2H),2.88(t, 2H,*J*=6Hz),3.27(s,2H,CH_2),4.32(brs,1H,NH),6.69(s,1H,OH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 22.77,22.80,24.77,28.21,37.93,41.48,62.26,77.32,155.88.
Anal.Calcd for $C_{12}H_{25}NO_3$:C,62.30;H,10.89;N,6.05. Found: C,62.55;H,11.07;N,6.78.

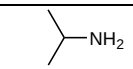
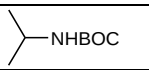
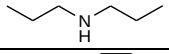
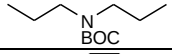
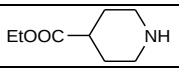
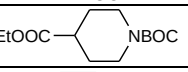
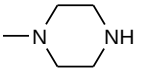
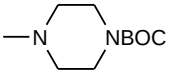
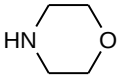
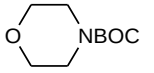
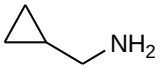
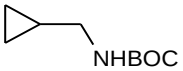
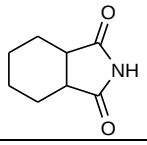
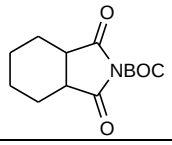
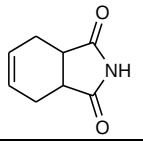
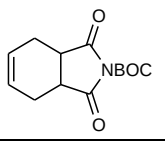
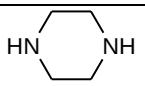
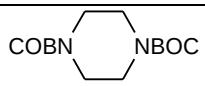
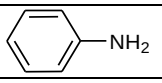
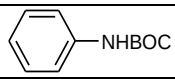
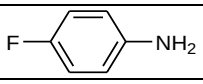
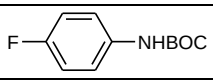
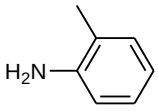
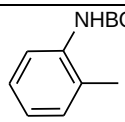
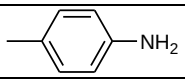
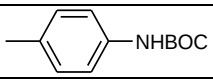
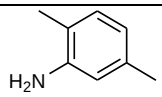
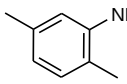
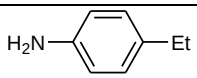
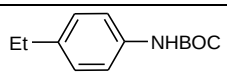
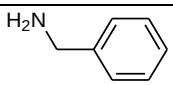
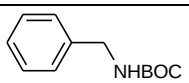
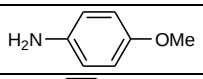
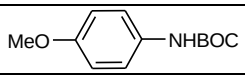
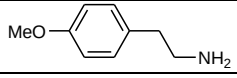
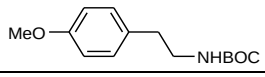
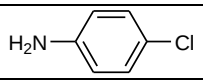
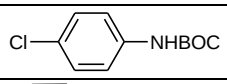
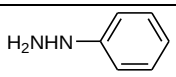
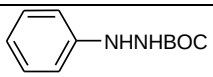
Tert-Butyl-2-hydroxyethyl Carbamate (Entry 33, Table-1):
^{1}HNMR(300MHZ,$CDCl_3$): δ_H1.45(s,9H,*t*-butyl),3.27(t,2H,*J*=4.8Hz,NCH_2),3.67(t,2H,*J*=4.8Hz,OCH_2),5.31(brS,1H).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C28.37,43.09,62.05,79.41,156.71.

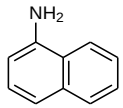
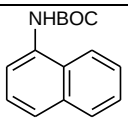
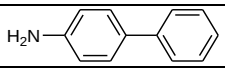
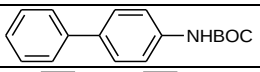
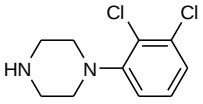
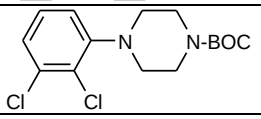
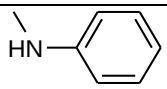
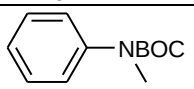
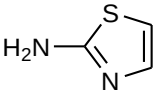
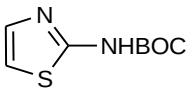
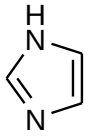
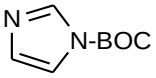
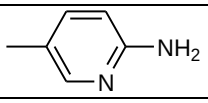
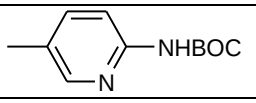
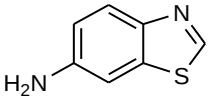
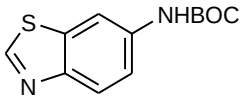
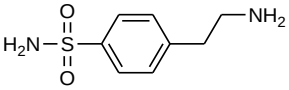
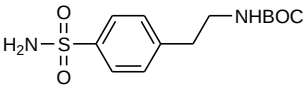
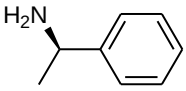
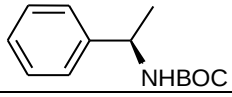
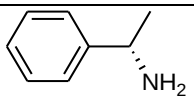
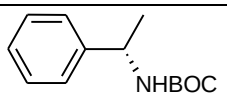
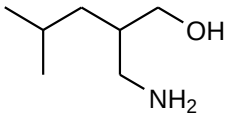
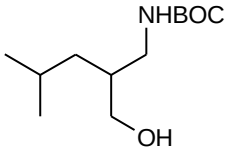
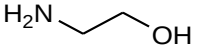
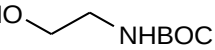
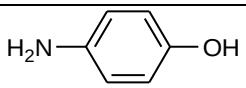
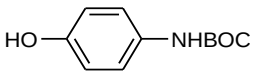
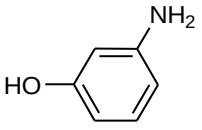
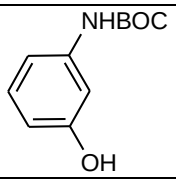
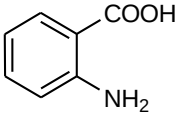
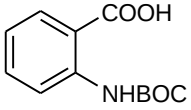
Tert-Butyl-4-hydroxy Phenyl Carbamate (Entry 34, Table-1):
Melting point: 139-142^{0}C. IR(KBr)cm^{-1}:1693.56.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.44(s,9H,*t*-butyl),6.63(d,2H,*J*=9Hz,Ar-H),7.20(d,2H,*J*=8.4Hz,Ar-H),8.98(brS,1H,NH),9.08(s,1H,OH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.14,78.41,114.97,119.99,130.95,152.45,152.98.

Tert-Butyl-3-hydroxyl Phenyl Carbamate (Entry 35, Table-1):
Melting point: 132-138^{0}C. IR(KBr)cm^{-1}:1693.58.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.46(s, 9H, t-butyl), 6.36-6.33(m, 1H, Ar-H), 6.82(d, 1H, *J*=8.1Hz, Ar-H), 7.01(d, 2H, *J*=7.8Hz, Ar-H), 9.20(brS,1H,NH),9.30(s,1H,OH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 28.08,78.80,105.23,108.96,109.11,129.16,140.51,152.64,157.54.

2-[(tert-Butoxy Carbonyl)amino] Benzoic acid (Entry 36, Table-1):
Melting point: 150-155^{0}C. IR(KBr)cm^{-1}:1728.28,1670.41.
^{1}HNMR(300MHZ,$CDCl_3$):δ_H1.47(s,9H,*t*-butyl),7.09-7.03(m,1H,Ar-H),7.59-7.53(m,1H,Ar-H),7.96(dd, 1H, *J*=8.1, 1.5Hz, Ar-H),8.28(dd,1H,*J*=8.7,0.9Hz,Ar-H),10.53(s,1H,COOH).
^{13}CNMR(300MHZ,$CDCl_3$): δ_C 27.86,80.10,115.06,117.98,121.41,131.20,134.21,141.47,151.96,169.61.

Table1. Protection of Various aromatic & aliphatic amines with Sodium Iodide

Entry	Amines	Products	Time(Min)	Yield(%)[a]
1			5/60[a]	93/82[a]
2			5	100
3			10	92
4			5/140[a]	98/78[a]
5			5/30[a]	96
6			5	98
7			30	94
8			30	93
9			5	90
10			30	95
11			40	94
12			45	94
13			45/150[a]	95/90[a]
14			45	95
15			45	94
16			15	95
17			15/90[a]	98/86[a]
18			30	96
19			90/150[a]	90/90[a]
20			15	98

21			90/130[a]	90/57[a]
22			40	97
23			40	95
24			5	100
25			25	95
26			10	98
27			10	96
28			60	91
29			30	90
30			60	95 $^{25}[\alpha]_D$ +55.04 (c=1,$CHCl_3$)
31			60	95 $^{25}[\alpha]_D$-57.8 (c=1,$CHCl_3$)
32			15	99
33			5	100
34			60	93
35			60	90
36			12h/ 24h[a]	80/--[a]

In comparison with Molecular Iodine[7]

RESULTS AND DISCUSSION

We recently presented that sodium iodide is readily available catalyst for affecting the protection of amines by the BOC group as tert-butyl Carbonates at room temperature(Scheme 1). Both Carbonyl oxygen atoms of BOC anhydride are activated by sodium iodide making the carbonyl group more susceptible to nucleophilic attack by amine 1 in one pot synthesis. This facilitates extrusion of tert-butanol and Carbon-di-oxide as leaving entities, leading to the formation of N-BOC derivatives of amines 3.
Further,the mechanical/activation of $(BOC)_2O$ by sodium iodide catalyzed N-BOC protection of amines was explored by IR(see supporting information), the IR frequency of a mixture of lequiv of NaI and lequiv of $(BOC)_2O$ was recorded. Two frequency bands of the C=O stretching vibration of carbonyl oxygen atoms were observed in the region of 1811.22 and 1623.15 cm^{-1}. where as the free carbonyl oxygen atoms of $(BOC)_2O$ at 1810.25 and 1755.28 cm^{-1}. (a doublet due to fermi resonance), the significant change in the vibration frequency indicated the feasible co-ordination of NaI with $(BOC)_2O$ where as I_2 was given in the region of 1807.33 and 1761.20 cm^{-1}.

The vigorous effervescence was observed after the addition of $(BOC)_2O$ to the amines within few seconds indicated the completion of the reaction and also the reactions were monitored by IR and TLC. No significant side products such as isocyanate, urea and N, N-diboc derivatives were observed and it was confirmed by IR and LC-MS[21]. Due to the better nucleophilicity of aliphatic amines, reaction rate was very faster. All the aliphatic primary and secondary amines (Table1; entry 1-9) gave the corresponding *N*-BOC amines in 92-98% yields in 5-15min, 1equiv of sodium iodide was used. Aromatic amines having different substitutents CH_3, F, OH, OCH_3 and Cl were converted to their N-t-BOC derivatives efficiently (entry 10-36, Table1).

Aromatic heterocycles are also protected efficiently and afforded good quantitative yields (entry 25-28, Table1). Aniline undergoes BOC protection at a much faster rate (20 min) in sodium iodide (1.0 equiv) compared to those methods using other lewis acids catalyzed protection strategies[5-10]. The presence of electron withdrawing groups in aromatic amines such as CN, COOMe, NO_2 etc. reduced the nucleophilicity of nitrogen of amino group significantly and hence we found no reaction at room temperature. We subjected these substrates at reflux, also no reaction.

The protection of amine group in anthranilic acid(entry 36, Table1) by BOC anhydride with sodium iodide gave the corresponding N-tert-boc derivative in 80% yield in comparison with molecular iodine [7], which is reported no reaction.

The chemoselectivity was demonstrated and the present protocol sodium iodide catalyzed N-BOC protection of amines were converted to the corresponding N-t-boc derivatives in excellent yields without any side products (entry 32-36, Table1) in very shorter duration[22].

The chiral amines (entry 30-31, Table1) gave optically pure N-BOC derivatives. The amine group is exclusively protected in comparatively good yields even in the presence of alchohol (entry 32-35, Table1).

CONCLUSION

We observed and found that the use of sodium iodide is much faster reaches rate for the protection of amines to afford corresponding N-t-boc derivatives.sodium iodide as a highly efficient catalyst for the protection of various electronically and structurally divergent open chain, cyclic aliphatic, aromatic and heteroaromatic amines as their corresponding N-t-boc derivatives at room temperature. This new protocol offers the following advantages: (1) It is inexpensive and readily available commercially (2) It has high chemoselectivity (3) shorter reaction times (4) high yields (5) It has no side products.

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