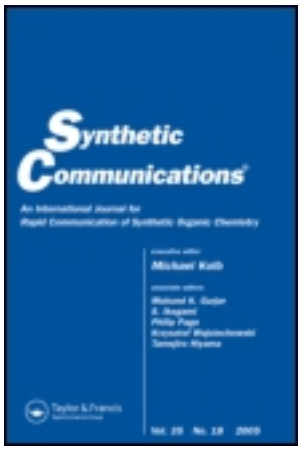

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INDIUM-MEDIATED BARBIER REACTIONS OF AZIDES: A FACILE SYNTHESIS OF N-ALLYLAMINE DERIVATIVES

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INDIUM-MEDIATED BARBIER REACTIONS OF AZIDES: A FACILE SYNTHESIS OF *N*-ALLYLAMINE DERIVATIVES

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ABSTRACT

N-Allylic amines are conveniently prepared in high yields by the reaction of azides with allylindium reagents in the presence of sodium iodide in DMF at ambient temperature.

Key Words: Indium reagents; Allylation; Azides; Allylamines

Organometallic reactions have found wide applications in organic synthesis.[1] In particular, organoindium reagents[2] have attracted much attention due to their compatibility with many organic functional groups (e.g., R–OH, CO_2R), stability and reactivity even in aqueous media. Further, indium mediated reactions exhibit a low nucleophilicity thus permitting chemoselective transformations of groups of similar reactivity. Allylindium reagents, generated in situ from allyl halides and indium

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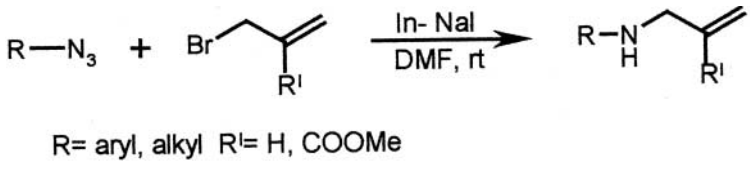
metal, react with various electrophiles[3,4] such as carbonyl compounds, C=N unsaturated systems, C–C multiple bonds, acyl halides, *gem*-diacetates and epoxides to generate homoallyl products. Aqueous solvents have proved to be most effective for indium-mediated reactions[5] and in certain cases significant regio-, diastereo- and even enantioselectivities have been achieved. Although, indium has been used extensively in carbonyl addition reactions it has not been used in the Barbier allylation reactions of azides. *N*-Allylamines are useful precursors for amino-Claisen rearrangement 6 and are generally prepared by reaction of allylbromide with primary amines in the presence of base. However, inspite of their potential utility, most of these procedures suffer from the formation of a mixture of products containing mono- and di-allylated products and also incompatibility with base sensitive substrates. The problems associated with these procedures can be overcome by the use of indium metal for this transformation.

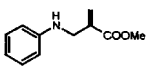
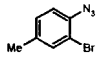
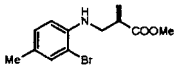
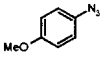
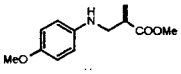
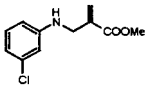
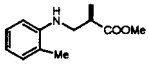
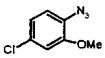
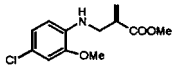
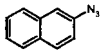
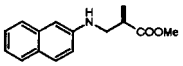
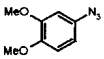
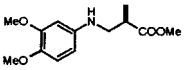
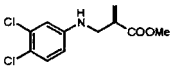
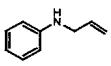
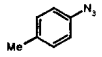
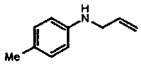
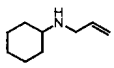
In continuation of our work on the applications of metals such as indium, magnesium, and zinc for various transformations,[7] we report here a novel and practical method for the preparation of *N*-allylamines through the indium-mediated allylation of azides. The treatment of phenyl azide with indium metal and methyl 2-(bromomethyl) acrylate in the presence of NaI in DMF gave exclusively mono-allylated ester in 80% yield (Scheme 1).

Similarly, several aromatic and aliphatic azides were reacted with methyl 2-(bromomethyl) acrylate and indium metal in DMF to afford the corresponding mono-allylaminoester derivatives in excellent yields. Further, the reactons of azides with allylindium bromide in the presence of NaI resulted in the formation of mono-*N*-allylamines in high yields with only a trace amount of corresponding *N*,*N*-diallylamine which was easily separated by column chromatography. The reactions proceeded smoothly at ambient temperature to give the products in high yields in a short reaction time. Unlike many zinc or tin promoted reactions that use acid catalyst, heat or sonication for inducing the reaction, this procedure does not require any stringent conditions or anhydrous solvent. Even though, this reaction proceeded smoothly in commercial DMF (containing 0.2% water) the reaction in water alone was not successful. The results as summarized in Table 1



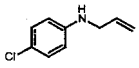
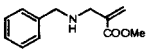
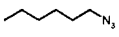
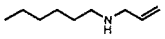
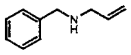
Scheme 1.

Table 1. Preparation of *N*-Allylamines Through Allylation of Azides

Entry	Azide (1)	Allyl Bromide	Product[a] (2)	Reaction Time (h)	Yield[b] (%)
a				1.5	80
b				2.0	85
c				1.0	87
d				2.5	81
e				3.0	84
f				2.5	80
g				3.5	75
h				3.0	89
i				2.5	80
j				2.0	90[c]
k				1.5	88[c]
l				2.5	73[c]

(continued)

Table 1. Continued

Entry	Azide (1)	Allyl Bromide	Product[a] (2)	Reaction Time (h)	Yield[b] (%)
m				3.0	85[c]
n				2.5	84
o				3.0	70[c]
p				2.0	80

[a]All products were characterised by ^{1}H NMR, IR and Mass spectra.
[b]Isolated yields after purification.
[c]5–8% di-allylated products were isolated.

clearly reveal the scope and generality of the reaction with respect to various alkyl and aryl azides. The formation of mono-*N*-allylamines may be attributed to the addition of allylindium reagent to the azide with successive loss of N_2 followed by proton capture during the work-up. The reactions were clean, high yielding and completed with in 1–3.5 h. Among various metals such as samarium, yttrium, zinc and bismuth studied for this transformation indium was found to be effective in terms of selectivity and conversion.

In summary, we have described a novel and convenient procedure for the preparation of mono-*N*-allylamines through the indium mediated Barbier allylation of azides. The procedure offers several advantages including high yields of products, short reaction times, cleaner reaction profiles, greater selectivity, simple experimental/product isolation procedures which makes it a useful and attractive strategy for the synthesis of mono-*N*-allyl amines.

EXPERIMENTAL

General Procedure

A mixture of azide (5 mmol), allylbromide or methyl 2-(bromomethyl) acrylate (7.5 mmol), indium powder (7.5 mmol) and sodium iodide (7.5 mmol) in DMF (15 mL) was stirred at room temperature for an appropriate time

(Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was quenched with saturated ammonium chloride (15 mL) and extracted with diethyl ether (2 × 15 mL). Evaporation of the solvent followed by purification on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 0.5–9.5) gave pure mono-*N*-allylamine.

Spectral data for products: 2a: ^{1}H NMR ($CDCl_3$) δ: 3.80 (s, 3H), 4.03 (s, 2H), 5.80 (s, 1H), 6.25 (s, 1H), 6.58 (d, 2H, $J = 7.8$ Hz), 6.65 (t, 1H, $J = 7.7$ Hz), 7.18 (t, 2H, $J = 7.8$ Hz). EIMS: *m/z*: 191 M^+, 158, 130, 106, 77, 41. IR (KBr): ν 3415, 2950, 1602, 1505, 1437, 1299, 1153, 952, 812, 750.

2b: ^{1}H NMR ($CDCl_3$) δ: 2.25 (s, 3H), 3.80 (s, 3H) 4.15 (s, 2H), 5.55 (s, 1H), 6.25 (s, 1H), 6.30 (m, 1H), 6.50 (m, 1H), 7.05 (m, 1H). EIMS: *m/z*: 283 M^+, 253, 224, 198, 172, 144, 117, 77. IR (KBr): ν 3405, 2932, 1617, 1515, 1444, 1233, 1139, 1024, 769.

2c: ^{1}H NMR ($CDCl_3$) δ: 3.70 (s, 3H), 3.80 (s, 3H), 4.18 (s, 2H), 5.80 (s, 1H), 6.23 (s, 1H), 6.23 (s, 1H), 6.70 (d, 2H, $J = 8.0$ Hz), 6.75 (d, 2H, $J = 8.0$ Hz). EIMS: *m/z*: 221 M^+, 205, 188, 174, 149, 136, 120, 77, 41. IR (KBr): ν 3410, 2937, 1620, 1517, 1450, 1237, 1144, 1030, 775.

2d: ^{1}H NMR ($CDCl_3$) δ: 3.80 (s, 3H), 4.15 (s, 2H), 5.60 (s, 1H), 6.25 (s, 1H), 6.50 (dd, 1H, $J = 8.0$ and 2.7 Hz), 6.55 (d, 1H, $J = 2.7$ Hz), 6.65 (d, 1H, $J = 8.0$ Hz), 7.05 (t, 1H, $J = 8.0$ Hz). EIMS: 225 M^+, 210, 193, 166, 140, 115, 99, 76. IR (KBr): ν 3420, 2945, 1608, 1515, 1435, 1295, 1148, 957, 820, 760. IR (KBr): ν 3418, 2953, 1605, 1515, 1440, 1296, 1157, 960, 815, 758.

2e: ^{1}H NMR ($CDCl_3$) δ: 2.23 (s, 3H), 3.75 (brs, NH), 3.83 (s, 3H), 4.18 (s, 2H), 5.80 (s, 1H), 6.28 (s, 1H), 6.58 (d, 1H, $J = 8.0$ Hz), 6.70 (t, 1H, $J = 7.8$ Hz), 7.10–7.18 (m, 2H). EIMS: *m/z*: 205 M^+, 190, 173, 144, 124, 120, 106, 91, 77, 65, 39. IR (KBr): ν 3420, 2968, 1616, 1520, 1450, 1295, 1157, 965, 825, 770.

2f: ^{1}H NMR ($CDCl_3$) δ: 3.80 (s, 3H), 3.83 (s, 3H), 4.03 (s, 2H), 4.65 (brs, NH), 5.80 (s, 1H), 6.30 (s, 1H), 6.40 (s, 1H), 6.58 (d, 1H, $J = 7.8$ Hz), 6.20 (d, 1H, $J = 8.0$ Hz). EIMS: *m/z*: 255 M^+, 224, 180, 154, 126, 99, 78, 39. IR (KBr): ν 3425, 2960, 1607, 1525, 1438, 1298, 1155, 960, 820, 760.

2g: ^{1}H NMR ($CDCl_3$) δ: 3.83 (s, 3H), 4.25 (s, 2H), 5.85 (s, 1H), 6.35 (s, 1H), 6.58 (d, 1H, $J = 7.8$ Hz), 7.25 (d, 1H, $J = 8.0$ Hz) 7.30 (d, 1H, $J = 8.0$ Hz), 7.43–7.50 (m, 2H), 7.80–7.87 (m, 2H). EIMS: *m/z*: 241 M^+, 209, 180, 154, 127, 115, 79, 41. IR (KBr): ν 3418, 2965, 1605, 1510, 1450, 1299, 1163, 950, 820, 765.

2h: ^{1}H NMR ($CDCl_3$) δ: 3.79 (s, 6H), 3.83 (s, 3H), 3.98 (s, 2H), 5.80 (s, 1H), 6.18 (d, 1H, $J = 7.8$ Hz), 6.20 (d, 1H, $J = 1.8$ Hz), 6.28 (s, 1H), 6.68 (d, 1H, $J = 7.8$ Hz). EIMS: *m/z*: 251 M^+, 235, 203, 153, 138, 110, 79, 41. IR (KBr): ν 3415, 2950, 1602, 1505, 1437, 1299, 1153, 952, 812, 753.

2i: ^{1}H NMR ($CDCl_3$) δ: 3.80 (s, 3H), 4.08 (s, 2H), 4.70 (brs, NH), 5.85 (s, 1H), 6.28 (s, 1H), 6.45 (d, 1H, $J = 8.0$ Hz), 7.02 (d, 1H, $J = 8.0$ Hz) 7.25 (d, 1H, $J = 2.0$ Hz). EIMS: m/z: 260 M^+, 228, 198, 174, 133, 111, 75, 55. IR (KBr): ν 3418, 2965, 1605, 1510, 1450, 1299, 1163, 950, 820, 765.

2k: ^{1}H NMR ($CDCl_3$) δ: 2.30 (s, 3H), 3.85 (m, 2H), 5.25–5.35 (m, 2H), 5.95 (m, 1H), 6.80 (d, 2H, $J = 8.0$ Hz), 7.35 (d, 2H, $J = 8.0$ Hz). IR (KBr): ν 3425, 2960, 1607, 1525, 1438, 1298, 1155, 960, 820, 760.

2n: ^{1}H NMR ($CDCl_3$) δ: 3.30 (s, 2H), 3.60 (s, 3H), 3.78 (s, 2H), 5.98 (s, 1H), 6.28 (s, 1H), 7.25–7.38 (m, 5H). EIMS: m/z: 205 M^+, 179, 141, 116, 107, 91, 69, 41. IR (KBr): ν 3415, 2950, 1602, 1505, 1437, 1299, 1153, 952, 812, 753.

2p: ^{1}H NMR ($CDCl_3$) δ: 3.80 (m, 2H), 5.20 (d, 1H, $J = 10.8$ Hz), 5.30 (d, 1H, $J = 16.8$ Hz), 5.90 (m, 1H), 6.45–6.55 (m, 2H), 6.60 (m, 1H), 7.05 (m, 1H). IR (KBr): ν 3410, 2960, 1615, 1510, 1440, 1305, 1160, 965, 826, 760.

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REFERENCES

1. (a) Li, C.-J. Tetrahedron **1996**, *52*, 5643; (b) Yamamoto, Y.; Asao, N. *Chem. Rev*. **1993**, *93*, 2207.
2. (a) Cintas, P. Synlett. **1995**, 1087; (b) Li, C.-J.; Chan, T.H. Tetrahedron **1999**, *55*, 11149.
3. (a) Paquette, L.A.; Mitzel, T.M. J. Am. Chem. Soc. **1996**, 118, 1931; (b) Loh, T.P.; Li, X.R. J. Chem. Soc. Chem. Commun. **1996**, 1929; (c) Issac, M.B.; Chan, T.H. J. Chem. Soc. Chem. Chem. **1995**, 1003.
4. (a) Loh, T.P.; Cao, G.Q.; Pei, J. Tetrahedron Lett. **1998**, *39*, 1453; (b) Bryon, V.J.; Chan, T.H. Tetrahedron Lett. **1997**, *38*, 6493; (c) Li, C.J.; Chen, D.L.; Lu, Y.Q.; Haberman, J.X.; Mague, J.T. J. Am. Chem. Soc. **1996**, *118*, 4216; (d) Chan, T.-H.; Lee, M.-C. J. Org. Chem. **1995**, *60*, 4228.
5. Li, C.-J.; Chen, T.H. Tetrahedron Lett. **1991**, *32*, 7017.
6. (a) Anderson, W.K.; Lai, G. Synthesis **1995**, 1287; (b) Yadav, J.S.; Reddy, B.V.S.; Rasheed, M.A.; Kumar, H.M.S. Synlett. **2000**, 487.
7. Yadav, J.S.; Srinivas, D.; Reddy, G.S.; Bindu, K.H. Tetrahedron Lett. **1997**, *38*, 8745; (b) Yadav, J.S.; Reddy, B.V.S.; Reddy, G.S.K.K. Tetrahedron Lett. **2000**, *41*, 2695; (c) Kumar, H.M.S.; Anjeneyulu, S.; Reddy, B.V.S.; Yadav, J.S. Synlett. **1999**, *5*, 551; (d) Yadav, J.S.; Reddy,

B.V.S.; Reddy, M.M. Tetrahedron Lett. **2000**, *4*, 2663; (e) Yadav, J.S.; Reddy, B.V.S.; Reddy, G.S.K.K. New Journal of Chemistry **2000**, *24*, 571; (f) Kumar, H.M.S.; Reddy, B.V.S.; Anjaneyulu, S.; Yadav, J.S. Tetrahedron Lett. **1999**, *40*, 8305.

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