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Convenient phosphorus tribromide induced syntheses of substituted 1-arylmethylnaphthalenes from 1-tetralone derivatives☆

Shagufta,[a] Resmi Raghunandan,[b] Prakas R. Maulik[b,†] and Gautam Panda[a,*]

[a]*Medicinal and Process Chemistry Division, Central Drug Research Institute, PO Box 173, Lucknow 226 001, India*
[b]*Molecular and Structural Biology Division, Central Drug Research Institute, PO Box 173, Lucknow 226 001, India*

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Abstract—A series of 1-arylmethylnaphthalenes **7a–g** and **11** have been synthesized conveniently in good yields at room temperature through phosphorus tribromide induced aromatization of 1-aryl-[3,4]-dihydronaphthyl-methanols **6a–g** and **10**, which were obtained from 1-tetralone derivatives.

Arylnaphthylmethane derivatives are important building blocks in organic synthesis. These compounds constitute the basic skeleton of many biologically important natural products and pharmaceuticals.[1] Naphthoyl and naphthylmethyl substituted Δ^8-tetrahydrocannabinol analogues **1** and **2** have cannabimimetic activity.[2] Naphthyl acetamides **3** are used for inhibiting secreted phospholipase A_2 (sPLA$_2$)-mediated release of fatty acids and in the treatment of conditions such as septic shock, adult respiratory distress syndrome, pancreatitis, trauma, bronchial asthma, allergic rhinitis and rheumatoid arthritis (Fig. 1).[3]

In continuation of our earlier work on aryl substituted methane derivatives,[4] we became interested in synthesizing substituted 1-arylmethylnaphthalenes, which are also a class of diarylmethanes. These classes of compounds have been prepared previously using different methods such as palladium catalyzed cross coupling between phenyl or naphthyl boronic acids and benzylic bromides,[5] copper catalyzed reactions of arylmagnesium derivatives with benzyl iodides,[6] nickel catalyzed cross coupling of arylphosphates with Grignard and organoaluminium reagents,[7] acid catalyzed rearrangement of cyclobutanols,[8] reduction of arylnaphthyl carbinols[9] or reduction of arylnaphthylketones.[10] These procedures describe syntheses of arylmethylnaphthalenes through functional group transformation or cross coupling reactions between two aromatic moieties. Additionally 1-substituted naphthalenes can be prepared from α-tetralone in acidic

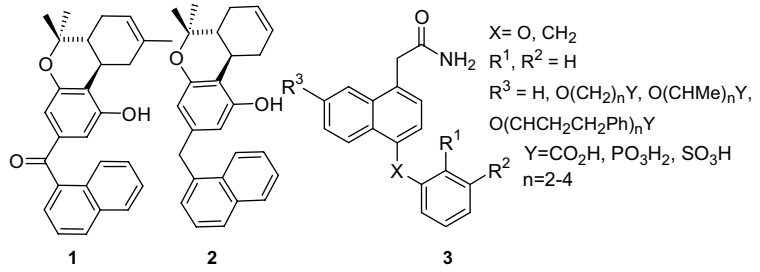

Figure 1. Structures of some biologically important arylmethylnaphthalene derivatives.

Keywords: Phosphorus tribromide; 1-Arylmethylnaphthalenes.
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* Corresponding author. Tel.: +91 5222364635; fax: +91 5222223938; e-mail addresses: bapi.rm@yahoo.com; gautam_panda@lycos.com
† For crystallographic queries.

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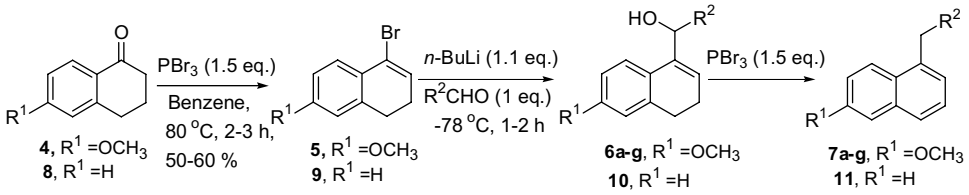
or basic medium by a xanthate mediated addition–cyclization sequence[11] and bromination of 1,1-dibenzyl tetralin derivatives.[12] We herein report a new and straightforward synthetic approach towards 1-arylmethylnaphthalene and its derivatives through facile aromatization of 1-aryl-[3,4]-dihydronaphthyl-methanols.

Treatment of 6-methoxy-1-tetralone **4** and 1-tetralone **8** with PBr_3 in dry benzene at 80 °C for 2–3 h furnished bromo derivatives **5** (60%) and **9** (50%), respectively. The lithio derivatives of **5** and **9** were synthesized by treatment with *n*-BuLi at −78 °C for 1 h in dry THF. The anion thus generated was reacted with several aldehydes (R^2CHO, R^2 = aryl and heteroaryl) to furnish a series of 1-aryl-3,4-dihydronaphthyl-methanols **6a**–**g** and **10** in 50–60% yields (Table 1).

It was anticipated that transforming the hydroxyl functionality in allyl alcohols **6a**–**g** and **10** into a leaving group might enforce aromatization through elimination of the leaving group from the α′-position of the dihydronaphthalene ring. Attempts to convert the hydroxyl functionality into a *p*-toluenesulfonyl group with *p*-TsCl were unsuccessful. Instead, PBr_3 was reacted with **6a**–**g** and **10** to transform the hydroxyl functionality into an $-OPBr_2$ group, which has been reported to effect aromatization[13] providing access to arylmethylnaphthalenes. To our delight, when allyl alcohols **6a**–**g** and **10** were reacted with PBr_3 at 0 °C, the reaction proceeded smoothly and efficiently, providing good yields of 1-arylmethylnaphthalenes **7a**–**g** and **11** (Table 1). The reaction was very fast and complete within 5–10 min and did not require any heating or drastic conditions.

Table 1. Synthesis of 1-arylmethylnaphthalenes **7a**–**g** and **11**



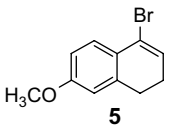
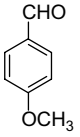
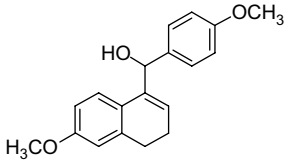
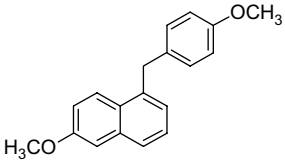
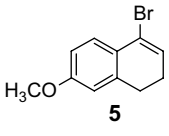
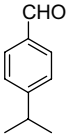
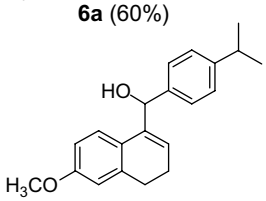
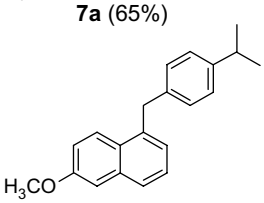
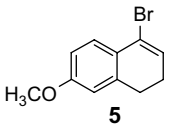
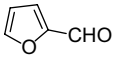
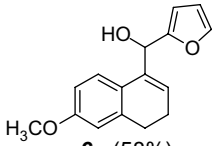
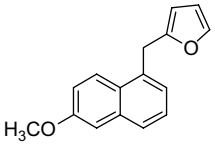
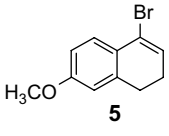
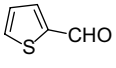
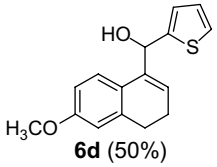
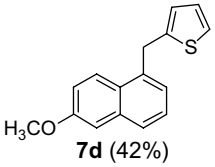
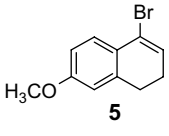
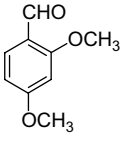
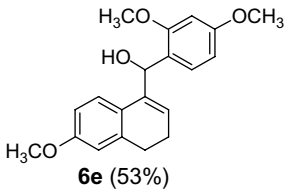
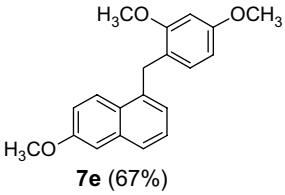
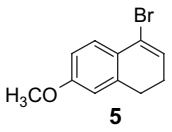
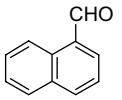
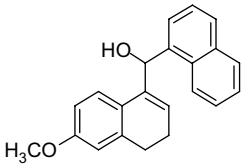
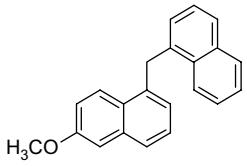
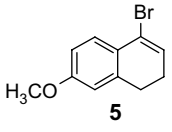
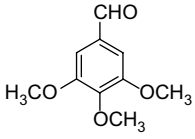
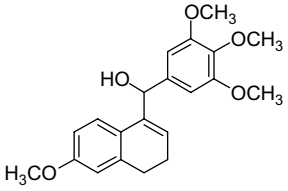
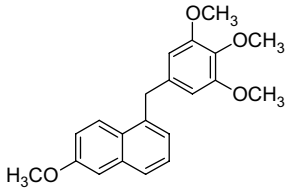
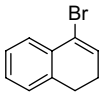
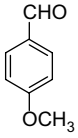
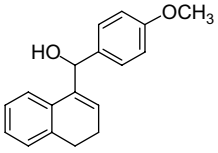
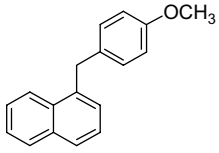
Entry	Substrate	R^2CHO	Carbinol yield (%)	Reaction conditions {PBr_3 (1.5 equiv) in dry benzene}	1-Arylmethylnaphthalene yield (%)
a	 **5**		 **6a** (60%)	0 °C, 5 min	 **7a** (65%)
b	 **5**		 **6b** (55%)	0 °C, 8 min	 **7b** (63%)
c	 **5**		 **6c** (58%)	0 °C, 6 min	 **7c** (49%)
d	 **5**		 **6d** (50%)	0 °C, 6 min	 **7d** (42%)
e	 **5**		 **6e** (53%)	0 °C, 5 min	 **7e** (67%)

Table 1 (*continued*)

Entry	Substrate	R^2CHO	Carbinol yield (%)	Reaction conditions {PBr_3 (1.5 equiv) in dry benzene}	1-Arylmethylnaphthalene yield (%)
f	 **5**		 **6f** (56%)	0 °C, 5 min	 **7f** (61%)
g	 **5**		 **6g** (53%)	0 °C, 5 min	 **7g** (55%)
h	 **9**		 **10** (60%)	0 °C, 5 min	 **11** (59%)

From close inspection of structures of **6a**–**g** and **10**, it was clear that the substituent R^2 could be an aryl or heteroaryl group. The reaction was independent of the substituent R^1 on the dihydronaphthalene ring of **6a**–**g** and **10**. Dehydrogenation of hydronaphthalenes is well known and is frequently the last step in the synthesis of aromatic hydrocarbons and their derivatives. The use of Pd/C, sulfur, selenium, DDQ and chloranil to effect aromatization is well established.[14] A catalyst, hydrogen acceptor, acidic conditions, high temperatures and long reaction times are usually required.[15,16] In these procedures, aromatization occurred through elimination of hydrogen or the leaving group from the di- or tetrahydro aromatic rings. Under our conditions, elimination of the leaving group from the α′-position of the ring B enforced aromatization furnishing **7a**–**g** and **11**.

The reaction can be thought to proceed via the formation of an intermediate **12**, formed through the reaction of allyl alcohols **6a**–**g** and **10** with PBr_3 followed by elimination of HBr, the intermediate **12** rearranging into the reactive quinoid **13**. Finally, **13** transforms into the more stable conjugated aromatic species **7a**–**g** or **11** (Scheme 1).

The structure of one of the 1-arylmethylnaphthalenes **7a** was confirmed through single crystal X-ray diffraction analysis.[17] Figure 2 shows the crystal structure and its conformation with the atomic numbering scheme used. The molecule contains a planar naphthalene with a methoxy group substituted at C3 and a 4-methoxy

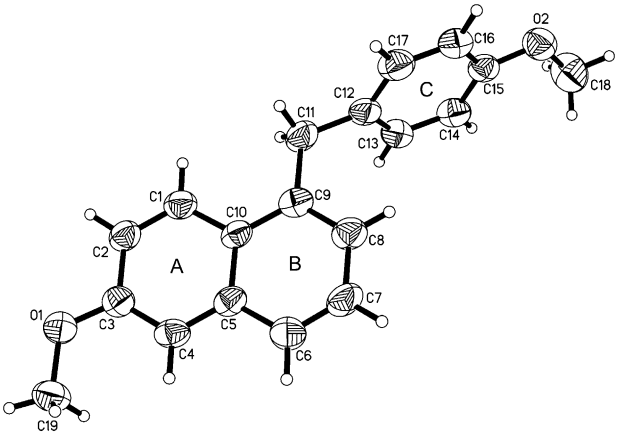
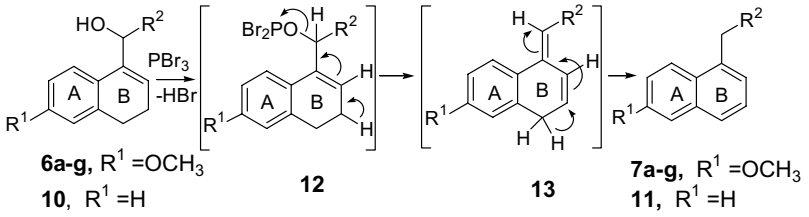


Figure 2. ORTEP diagram showing the molecular structure of **7a**.



Scheme 1. Possible reaction mechanism.

benzyl group at C9. The naphthalene and methoxy group at C3 are nearly planar while the twist angle between the least-squares mean plane of the 4-methoxy benzyl group and naphthalene ring is 79.9(1)°.

In summary, we have demonstrated that 1-arylmethylnaphthalenes **7a**–**g** and **11** can conveniently be synthesized from 1-tetralone and its derivatives in good yields. The procedure involves readily available inexpensive starting materials and a rare example of aromatization under extremely mild conditions (0 °C, 5–8 min). The procedure can be applied to combinatorial synthesis of various 1-arylmethylnaphthalenes and work towards this direction is underway.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.06.016.

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17. Crystal data for **7a**: $C_{19}H_{18}O_2$, $M = 278.33$, Monoclinic, $P2_1/n$, $a = 9.805(2)$, $b = 5.482$ (1), $c = 27.984(4)$ Å, $\beta = 91.74(1)°$, $V = 1503.5(5)$ Å^3, $Z = 4$, $D_c = 1.230$ g cm^{-1}, μ(Mo-K$_\alpha$) = 0.078 mm^{-1}, $F(0\,0\,0) = 592$, colourless crystal, size: $0.6 \times 0.35 \times 0.4$ mm, 3857 reflections measured (1071 unique), $Rw = 0.2002$ for all data, $R = 0.0891$ $wR2 = 0.2405$ for 2663 on F values of reflections with $I > 2\sigma(I)$, $S = 1.037$ for all data and 193 parameters. Unit cell determination and intensity data collection ($2\theta = 50°$) were performed on a Bruker P4 diffractometer at 293(2) K. The structure was solved by direct methods and refinements were made by full-matrix least-squares methods on F^2. Programs: XSCANS [(Siemens Analytical X-ray Instrument Inc.: Madision, WI, USA, 1996) was used for data collection and data processing], SHELXTL-NT [(Bruker Axs Inc.: Madison, WI, USA, 1997) was used for structure determination, refinements and molecular graphics]. Further details of the crystal structure investigation can be obtained from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB21EZ, UK (CCDC deposition No: 272578).
Typical procedure for **7a**–**g** and **11**: To a solution of carbinol **6a**–**g** or **10** {0.100 g (1 equiv)} in dry benzene (5 mL) at 0 °C was added PBr_3 (1.5 equiv) and the mixture was stirred at room temperature. After completion of reaction, the mixture was poured into ice-cold water and extracted with ethyl acetate. Column chromatography of the crude product over silica gel (ethyl acetate/hexane) furnished compounds **7a**–**g** and **11**.
Selected spectral data:
2-(6-Methoxynaphthalen-1-ylmethyl)furan **7c**: IR (Neat): 2928, 2365, 1220, 1025, 769 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.90 (s, 3H, OC*H*$_3$), 4.36 (s, 2H, ArC*H*$_2$), 5.89 (d, 1H, $J = 2.9$ Hz, furyl *H*), 6.25 (dd, 1H, $J_1 = 3.0$ Hz, $J_2 = 1.9$ Hz, furyl *H*), 7.15–7.24 (m, 3H, Ar*H*), 7.32–7.41 (m, 2H, furyl *H*, Ar*H*), 7.65 (d, 1H, $J = 8.1$, Ar*H*), 7.9 (d, 1H, $J = 9.4$, Ar*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ 34.7, 56.0, 105.7, 110.4, 118.2, 124.1, 125.1, 125.3, 126.9, 128.4, 133.9, 134.6, 141.5, 152.5, 157.4. MS (FAB): *m*/*z* (%) 238 (100), [M$^+$], 171 (55), [M$^+$−C$_4$H$_3$O]. Anal. $C_{16}H_{14}O_2$; Calcd: C, 80.65; H, 5.92. Found: C, 80.92; H, 5.99.
1-(2,4-Dimethoxybenzyl)-6-methoxynaphthalene **7e**: IR (KBr): 3009, 3938, 1611, 1506, 1260, 1213, 1156, 1041, 758 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.75 (s, 3H, OC*H*$_3$), 3.84 (s, 3H, OC*H*$_3$), 3.90 (s, 3H, OC*H*$_3$), 4.29 (s, 2H, ArC*H*$_2$Ar), 6.29 (dd, 1H, $J_1 = 2.4$ Hz, $J_2 = 8.2$ Hz, Ar*H*), 6.50 (d, 1H, $J = 2.2$ Hz, Ar*H*), 6.70 (d, 1H, $J = 8.4$ Hz, Ar*H*), 7.15–7.10 (m, 3H, Ar*H*), 7.35 (t, 1H, $J = 7$ Hz, Ar*H*), 7.62 (d, 1H, $J = 8.2$ Hz, Ar*H*), 7.88 (d, 1H, $J = 9$ Hz, Ar*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ 32.3,

55.7, 55.8, 98.7, 104.3, 106.9, 118.7, 121.8, 125.3, 126.1, 126.4, 126.6, 128.2, 130.6, 135.5, 137.4, 157.6, 158.3, 159.7; MS (FAB): *m/z* (%) 308 (100), [M^+], 171 (70), [$M^+-(OCH_3)_2C_6H_3$], Anal. $C_{20}H_{20}O_3$; Calcd: C, 77.90; H, 6.54. Found: C, 77.95; H, 6.58.

1-(4-Methoxybenzyl)naphthalene **11**: IR (KBr): 3435, 1597, 1507, 1244, 1029, 796 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 3.76 (s, 3H, OCH_3), 4.38 (s, 2H, $ArCH_2Ar$), 6.79 (d, 2H, J = 8.6 Hz, Ar*H*), 7.11 (d, 2H, J = 8.54, Ar*H*), 7.26 (d, 1H, J = 6.6 Hz, Ar*H*), 7.47–7.41 (m, 3H, Ar*H*), 7.74 (d, 1H, J = 8.2 Hz, Ar*H*), 7.84 (m, 1H, Ar*H*), 7.99 (m, 1H, Ar*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ 38.5, 55.6, 114.3, 124.7, 125.3, 126.3, 127.5, 130.1, 132.5, 133.1, 134.3, 137.5, 158.3; MS (FAB): *m/z* (%) 248 (100), [M^+], 141 (80), [$M^+-OCH_3C_6H_4$] Anal. $C_{18}H_{16}O$; Calcd: C, 87.06; H, 6.49. Found: C, 87.10; H, 6.45.