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A facile synthesis of naphthyl ethers using micellar medium

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ABSTRACT

In the present investigation a series of naphthyl ethers have been synthesized by the micellar mediated reactions of naphthols with equimolar mixture of phenacyl or benzyl bromide-triethylamine in 70% methanol/water (v/v) at 30^0 C. The structures of the compounds have been confirmed by elemental and spectral analysis. The compounds have also been screened for their antimicrobial activities.

Keywords: Naphthyl ether, Naphthol, Phenacyl bromide,Benzyl bromide, Antimicrobial activity.

INTRODUCTION

Benzyl and phenacyl groups are commonly employed for the protection of alcohol, phenol and naphthol moieties[1]. Benzyl ethers act as intermediates in sigmatropic rearrangement reactions such as Claisen and Cope rearrangements[2]. Since benzyl and phenacyl ethers of naphthols are aromatic ethers, they are expected to find wide application in the field of pharmaceuticals as drugs and in agrochemicals as herbicide and fungicides. Aromatic ethers are also found application in chemical engineering[3], food coloring, perfumery and in medicines[4].

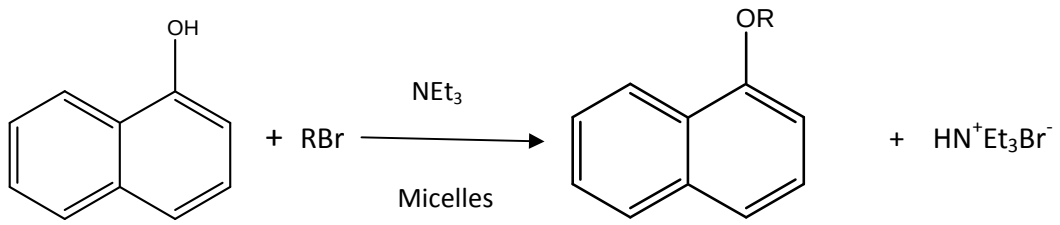
Naphthyl ethers can be conveniently prepared from the naphthols using benzyl bromide or phenacyl bromide[5]. Phenacyl bromide or benzyl bromide in combination with triethyl amine in a micellar medium are frequently employed for the generation of phenacyl and benzyl ethers respectively from naphthols[6].

It was mainly considered to protect naphthol with phenacyl or benzyl group in the presence of micellar medium and found that alcohol protection can be carried out efficiently with phenacyl or benzyl with triethyl amine by the use of micellar medium[7]. Nallu et have so for reported synthesis of few phenolic ethers using micellar medium, however, the reaction required mild conditions at room temperature[8]. The structures of the compounds synthesized in this work have been assigned on the basis of elemental analysis, IR , ^{1}H NMR and ^{13}C NMR spectral data. In continuation of our studies and the biological activity[9], these compounds have also been screened for their antimicrobial activities and the results discussed in Table2.

EXPERIMENTAL SECTION

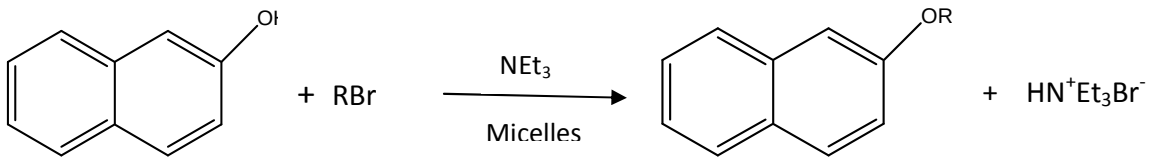
Melting points were determined in open capillaries on a Thomas Hoover apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker WH 500 spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical Shifts are given in parts per million (ppm). Splitting patterns are designated as follows: s- singlet, d- doublet, t-triplet, q-quartet and m- multiplet. Mass spectra (MS) were recorded on Shimadzu LC-MS. The reactions were followed on precoated TLC plates (Silica gel 60 F254, Merck) visualizing the spots in iodine chamber.

Scheme-1



	R
1a.	$-CH_2\ C_6H_5$
1b.	$-CH_2\ C_6H_4\ NO_2$-*p*
1c.	$-CH_2COC_6H_5$
1d.	$-CH_2COC_6H_4NO_2$-*p*

Scheme-2



	R
1a.	$-CH_2\ C_6H_5$
1b.	$-CH_2\ C_6H_4\ NO_2$-*p*
1c.	$-CH_2COC_6H_5$
1d.	$-CH_2COC_6H_4NO_2$-*p*

Target compounds were prepared according to Scheme **1 & 2**. Reaction of naphthols with phenacyl, benzyl bromides and its substituted bromide in presence of micellar medium gave naphthyl ethers. Formation of naphthyl ether was confirmed by appearance of IR band in the region 1216 cm^{-1} indicating C-O-C ether linkage in the compounds **(1a-1d)** and **(2a-2d).** Phenacyl naphthyl ether shows this band at 1223cm^{-1}. The slight increase in the frequency may be attributed to the more delocalization of the unshared pair of electrons of oxygen in to the naphthyl ring. For the compound **2c**, this frequency appears at 1260cm^{-1}. This may be due to the presence of electron withdrawing $–NO_2$ group at para- position of benzene ring. The absorbtion frequency of C=O group of phenacyl ethers **1c,1d,2c** and **2d** occurs at 1690 – 1704 cm^{-1}. This observed value is less than that of the saturated aliphatic ketone (1715cm^{-1}) ,this decrease may be due to the conjugation of the carbonyl group with aromatic ring which lengthens the C=O bond . The –C=N stretching vibration appears at 861 cm^{-1}. ^{1}H-NMR spectra showed a singlet at 5.9 ppm due to methylene proton (-CH_2-O-) of naphthyl ether. The other chemical shift values are found to be comparable to the reported values of similar compounds[8]. The –CH_2-O- signal moves further to downfield 5.9 ppm for the compound **2d**. This may be due to the presence of electron withdrawing $–NO_2$ group at 4-position of benzene ring. Similarly ^{13}C-NMR spectra showed a signal at 77.7 ppm due to –O-CH_2 of phenacyl ether. The synthetic routes of above mentioned compounds are shown in Scheme-1 & 2.

Preparation of naphthyl ethers (1a-1d) and (2a-2d)

A mixture of 1-naphthol (0.1 mol) , triethyl amine (0,1mol) and benzyl bromide (0.1 mol) in micellar medium were stirred for 30 minutes at 30 C `and kept overnight at room temperature. The solid product obtained was filtered, washed with water and recrystallised from ethanol to get benzyl naphthyl ether.

1a. Benzyl-1-naphthyl ether: Yield 70% mp:81 C IR(cm^{-1}): 3062 (aromatic ring –CH), 1227 (C-O-C), 1598 (C=C), 2918(aliphatic –CH) cm^{-1}.^{1}H NMR (ppm): 8.2 (7H, m, naph), 7.4 (5H,m, -CH_2Ph), 5.3 (2H,s, -OCH_2); ^{13}C NMR (ppm): 70.4, 77.8, 107.5, 119.4, 124.1, 126.4, 127.2, 128.6, 129.8, 134.9, 137.2, 157.5. Mass (m/z):234 (M^+ peak).

1b. 4-nitrobenzyl-1-naphthyl ether: Yield (65%), MP 148 C; IR(cm^{-1}): 3043 (aromatic –CH), 1239 (C-O-C), 1578 (C=C) cm^{-1}. ^{1}H NMR (ppm): 8.4 (7H,m, naph), 7.6 (4H, -$CH_2C_6H_4NO_2$-P), 5.4 (2H,s, -OCH2); ^{13}C NMR(ppm): 71.2, 78.1, 108.5, 120,4, 123.5, 126.2, 127.1, 128.4, 129.2, 133.2, 157. Mass(m/z):279 (M^+ peak).

1c. Phenacyl-1-naphthyl ether: Yield (62%), MP 56 C; IR(cm^{-1}): 3000 (aromatic ring -CH), 1223 (C-O-C), 1595 (C=C), 2940 (aliphatic –CH),cm^{-1}; ^{1}H NMR (ppm); 8.3 (7H,m, naph), 7.5 (5H, m, -CO CH_2Ph), 5.5 (2H,s, -OCH_2); ^{13}C NMR (ppm); 70.1, 71.5, 107.2, 118.2, 124.1, 125.4, 127.5, 128.1, 129.9, 133.8, 155.9. Mass (m/z):262 (M^+ peak).

1d. 4-nitrophenacyl-1-naphthyl ether: Yield (71%), MP 172 C; IR(cm^{-1}): 3040 (aromatic ring –CH), 1227 (-C-O-C), 1690 (C=O), 2920 (aliphatic –CH)cm^{-1}; ^{1}H NMR (ppm): 8.4 (7H, m, naph), 8.2 (4H, m, -COC_6H_4-NO_2-P), 5.8 (2H, s, -OCH_2): ^{13}C NMR(ppm): 70.5, 71.9, 109.1, 119.2, 124.8, 126.2, 128.2, 128.5, 129.2, 134.5, 153.2: Mass(m/z): 307 (M^+ peak).

2a. Benzyl-2-naphthyl ether: Yield(67%), MP 91 C; IR(cm^{-1}): 3057 (aromatic ring –CH), 1217 (C-O-C), 2920 (aliphatic –CH), 1598 (C=C)cm^{-1}; ^{1}H NMR (ppm): 8.3 (7H, m, naph), 7.5 (5H, m, -CH_2Ph), 5.2 (2H, s, -OCH_2); ^{13}C NMR (ppm): 70.6, 77.2, 107.1, 118.9, 124.5, 126.7, 127.8, 128., 129.2, 134.1, 137.2, 157.4; Mass(m/z):234 (M^+ peak).

2b. 4-nitrobenzyl-2-naphthyl ether: Yield(56%), MP 109 C; IR(cm^{-1}): 3050 (aromatic ring –CH), 1220 (C-O-C), 2905 (aliphatic –CH), 1600 (C=C)cm^{-1}. ^{1}H NMR (ppm): 7.8 (7H, m, naph), 7.2 (4H, m, -$CH_2C_6H_4NO_2$-P), 5.3 (2H, s,-OCH_2); ^{13}C NMR(ppm): 71.0, 78.3, 108.3, 120.6, 123.1, 126.4, 127.4, 128.6, 129.4, 133.0, 157.5. Mass (m/z):279 (M^+ peak).

2c. Phenacyl-2-naphthyl ether: Yield(69%), MP 102 C; IR(cm^{-1}): 3058 (aromatic ring –CH), 1228 (-C-O-C-), 2897 (aliphatic –CH), 1599 (C=C), 1704 (C=O) cm^{-1}; ^{1}H NMR (ppm); 8.2 (7H, m, naph), 7.5 (5H, m, -$CH_2COC_6H_5$), 5.4 (2H, s, -OCH_2); ^{13}C NMR (ppm): 70.2, 71.7, 107.4, 118.5, 124.2, 125.4, 127.3 128.3 128.6 129.5 133.7, 155.5; Mass (m/z):262 (M^+ peak).

2d. 4-nitrophenacyl-2-naphthyl ether: Yield(57%), MP 182 C; IR(cm^{-1}): 3108 (aromatic ring –CH), 1222 (C-O-C), 2913 (aliphatic –CH), 1605 (C=C), 1690 (C=O) cm-1; ^{1}H NMR (ppm): 8.2 (7H, m, naph), 8.0 (4H, m, -$CH_2COC_6H_4NO_2$-P), 5.5 (2H, s, -OCH_2); ^{13}C NMR (ppm): 70.6, 71.5, 109.3, 119.6, 124.2, 126.4, 128.1, 128.7, 129.0, 134.9, 153.9; Mass(m/z):307 (M^+ peak).

Table 1: Elemental analysis of Compounds (1a-1d) & (2a-2d)

Compd No	Molecular formula	R	Elemental Analysis (%)					
			Calculated			Found		
			C	H	N	C	H	N
1a	$C_{18}H_{14}O_2$	-$CH_2C_6H_5$	82.48	5.37		82.44	5.34	
1b	$C_{18}H_{14}O_4N$	-$CH_2C_6H_4$-NO_2-P	70.10	4.52	25.38	70.13	4.55	25.32
1c	$C_{17}H_{14}O$	-CH_2-CO-C_6H_5	87.16	5.94		87.13	5.98	
1d	$C_{17}H_{14}O_3N$	-CH_2-CO-C_6H_4-NO_2-P	72.83	5.03	22.11	72.85	5.00	22.15
2a	$C_{18}H_{14}O_2$	-$CH_2C_6H_5$	82.46	5.36		82.44	5.34	
2b	$C_{18}H_{14}O_4N$	--$CH_2C_6H_4$-NO_2-P	70.15	4.52	25.33	70.13	4.55	25.32
2c	$C_{17}H_{14}O$	-CH_2-CO-C_6H_5	87.11	5.96		87.13	5.98	
2d	$C_{17}H_{14}O_3N$	-CH_2-CO-C_6H_4-NO_2-P	72.86	4.98	22.16	72.85	5.00	22.15

Table 2 : Antimicrobial activity of compounds, zone of inhibition in mm

Compounds	*B.cereus*	*S.aureus*	*A.flaves*	*A.niger*
1a	9	12	9	11
1b	15	11	14	11
1c	13	14	11	12
1d	20	18	11	12
2a	12	10	16	16
2b	10	11	13	14
2c	11	11	12	10
2d	12	14	14	9

Antimicrobial activity

The compounds **(1a-1d)** and **(2a-2d)** were screened for their antibacterial activity against *bacillus cerus* and *proteus mirabillis* and *proteus`mirabilis* and antifungal activity against *aspergillus flaves* and *aspergillus niger* at a concentration of 60ug/ml in DMSO by cup-plate method, zone of inhibition in mm[10,11].The results are given in Table-2.

CONCLUSION

A series of naphthyl ethers **(1a-1d)** and **(2a-2d)** have been newly synthesized and the structures confirmed by elemental analysis and spectral analysis. Most of the synthesized compounds have shown antibacterial and antifungal activity to some extent. Among the compounds **1b** and **1c** show considerable activity while rest show feeble activity against *B.cereus*. However, the compound **1c** shows significant activity against *B.cereus* compound **1c** show moderate activity against *proteus mirabilis* **1d** shows significant activity against the same and others show feeble activity against *proteus mirabilis*. The compound **2a** shows significant activity while compounds **1c,1d** and **2a** show moderate activity against *aspergillus niger*. Again the compound **2a** shows reasonable activity against *Aspergillus flaves*.

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