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Research Article

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Micelles as catalyst for the synthesis of certain substituted naphthyl ethers

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ABSTRACT

Surfactants, above their critical micelle concentration, in aqueous-organic media were found to be a highly efficient catalyst for the synthesis of aromatic ethers in the presence of an organic base like triethylamine at room temperature. This method may also be used for selective o-alkylations.

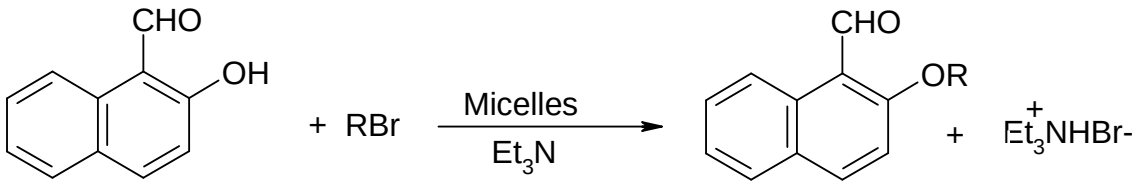
Key words: aromatic triethylamine, micelles, antimicrobial activity.

INTRODUCTION

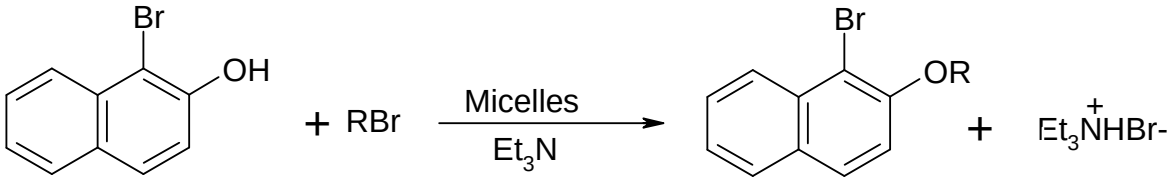
The Williamson reaction is a conventional method for transformation in organic synthesis since the products are of value in both academic and industrial applications.[1a-c] ‘ The Williamson synthesis usually involves the employment of an alkali-metal salt of the hydroxy compound and an alkyl halide. These reactions are usually performed using organic solvents[2] in the presence of inorganic base followed by refluxing for several hour. There are a few useful procedures available for the conversion of phenols into aromatic ethers, which do not require initial formation of phenoxide ion.[3-5] It is known that a variety of organic reactions are catalyzed or inhibited by micelles in the organic media.[6-7] Here,we have used anionic surfactant in the reaction of substituted phenacyl / benzyl bromide with equimolar mixture of substituted naphthols-triethylamine in the course of our investigation on micellar catalyzed reaction with a view of knowing more effective method for etherification. In our earlier communications we have reported that micelles were found to be an efficient catalyst[10] for the synthesis of unsubstituted napthyl ether.

EXPERIMENTAL SECTION

All the reagents and solvents used were of labased on the data shown inboratory grade. The melting points of the compounds were determined by open capillaries on a Thomas Hoover apparatus and uncorrected. The purity of the products were tested by TLC technique. The structure of these compounds were supported by their IR, ^{1}H, ^{13}C NMR, Mass spectral data and C, H, N analytical data. The assignment of the spectral data was made based on the literature values.[11] In the investigation of our studies on the biological activity, these compounds have also been screened for their antimicrobial activities and the results discussed in Table 3.



1a –CH_2–COC_6H_5
1b –CH_2–$COC_6H_4NO_2$-*p*
1c –CH_2–C_6H_5
1d –CH_2–$C_6H_4NO_2$-*p*



2a –CH_2–COC_6H_5
2b –CH_2–$COC_6H_4NO_2$–*p*
2c –CH_2–C_6H_5
2d –CH_2–$C_6H_4NO_2$–*p*

Scheme-1

Synthesis and characterization of compounds

Equimolar mixture of naphthol(s) triethylamine was treated with phenacyl / benzyl bromide(s) in the presence of anionic surfactant sodium lauryl sulphate (NaLS) in methanol-water 70% (v/v). The reaction mixture was kept at 30^{o}C and stirred continuously for an hour. The solid product was isolated and recrystallized using methanol. The synthetic route of the compounds (1a-1d & 2a-2d) is shown in Scheme-1.

RESULTS AND DISCUSSION

The compounds (1a-1d) & (2a-2d) prepared in the present work are new to the literature. The substituted phenacyl/benzyl naphthyl ethers have been prepared in an excellent yield probably by the following pathway of the reaction. The -$COCH_2Br$, –CH_2Br part of $PhCOCH_2Br$ / $PhCH_2Br$ and OH group of naphthol(s) may be highly exposed in the hydrophilic region, where as aromatic part of the reactants may be populated in the hydrophilic region of the micelles. In this situation, triethylamine may act as co-surfacant. The reaction may be facilitated at the interface of the micelles.

Table 1. Physical data of compounds 1a - 1d & 2a-2d

Compound No.	R	M - F	MP (^{o}C)	Yield (%)	R_f values
1a	–CH_2–COC_6H_5	$C_{19}H_{14}O_3$	182 - 184	75	0.49
1b	–CH_2–$COC_6H_4NO_2$	$C_{19}H_{13}O_5N$	110 - 112	76	0.48
1c	–CH_2–C_6H_5	$C_{18}H_{14}O_2$	171 - 172	77	0.57
1d	–CH_2–$C_6H_4NO_2$	$C_{18}H_{13}O_4N$	155 - 157	75	0.46
2a	–CH_2–COC_6H_5	$C_{18}H_{13}O_2Br$	105 - 107	79	0.50
2b	–CH_2–$COC_6H_4NO_2$	$C_{18}H_{12}O_4NBr$	108 - 111	70	0.48
2c	–CH_2–C_6H_5	$C_{17}H_{13}OBr$	95 - 97	80	0.58
2d	–CH_2–$C_6H_4NO_2$	$C_{17}H_{12}O_3NBr$	135 – 137	70	0.55

Table 2. Elemental analysis of compounds 1a - 1d & 2a-2d

Compound No.	R	M - F	Calculated			Found		
			C	H	N	C	H	N
1a	–CH_2–COC_6H_5	$C_{19}H_{14}O_3$	78.62	4.82	-	78.51	4.93	-
1b	–CH_2–$COC_6H_4NO_2$	$C_{19}H_{13}O_5N$	68.05	3.88	4.17	70.12	4.08	4.52
1c	–CH_2–C_6H_5	$C_{18}H_{14}O_2$	82.14	5.34	-	82.56	5.45	-
1d	–CH_2–$C_6H_4NO_2$	$C_{18}H_{13}O_4N$	70.35	4.23	4.46	70.21	4.34	4.30
2a	–CH_2–COC_6H_5	$C_{18}H_{13}O_2$	63.34	3.81	-	63.10	3.20	-
2b	–CH_2–$COC_6H_4NO_2$	$C_{18}H_{12}O_4N$	55.95	3.10	3.62	56.10	3.22	4.08
2c	–CH_2–C_6H_5	$C_{17}H_{13}O$	65.17	4.15	-	65.31	4.28	-
2d	–CH_2–$C_6H_4NO_2$	$C_{17}H_{12}O_3N$	56.98	3.35	3.91	56.84	3.47	3.79

Table 3. Antimicrobial activity of compounds - zone of inhibition in mm

Compound No.	*B. cereus*	*S. aureus*	*A. hyrophila*	*P. mirabilis*	*A. flaves*	*A. niger*
1a	39	29	14	35	30	37
1b	25	28	22	24	32	37
1c	20	20	13	24	25	25
1d	28	31	30	29	20	16
2a	32	26	24	35	14	16
2b	27	35	24	28	20	16
2c	13	14	14	18	13	11
2d	26	34	28	36	30	25
Gentamycin	40	42	-	38	-	-
Miconozole	-	-	-	-	40	

1a. 2-(2-Oxo-1-phenylethoxy)naphthalene-1-carbaldehyde; Yield - 75%, M.P. 182 – 184 ^{o}C, R_f - 0.49(Ethylacetate:methanol 1:1); IR (KBr) cm^{-1}: 3088(aromatic –CH str),2845(aliphatic –CH str), 1704 (C=O str), 1653(aldehydic - CHO str) & 1220 (C–O–C str) ;^{1}H NMR($CDCl_3$) ppm: 10.24 (s, 1H, -CHO), 8.08 (m, 6H,naph), 7.45 (m, 5H, -$COCH_2C_6H_5$), 5.29 (s, 2H, –O–CH_2) ppm; ^{13}C NMR ($CDCl_3$) ppm: 194.31, 190.28, 154.64, 151.92, 139.32, 136.62, 135.95, 130.92, 130.32, 129.16, 128.92, 128.17, 127.97, 125.70, 123.37, 122.92, 115.38, 102.78 & 72.26 ppm. Mass(m/z): 289(M^+ peak).

1b. 2-[2-Oxo-2-(4-nitrophenylethoxy)naphthalene-1-carbaldehyde: Yield - 75%, M.P. 155 - 157 ^{o}C, R_f - 0.46 (Ethylacetate :methanol 1:1); IR (KBr) cm^{-1} : 3075(aromatic –CH str),2922(aliphatic –CH str), 1720 (C=O str), 1649 (aldehydic -CHO str),1220 (C–O–C str) & 810(-NO_2 str);^{1}H NMR($CDCl_3$) ppm: 10.28 (s, 1H, -CHO), 8.12(m, 6H,naph), 7.25 (m, 4H, -$COCH_2C_6H_4NO_2$-*p*), 5.68 (s, 2H, –O–CH_2) ppm;^{13}C NMR ($CDCl_3$) ppm:197.31, 192.28, 157.64, 153,92, 141.32, 138.62, 136.95, 133.18, 131.32, 129.78, 129.16, 128.72, 128.10, 127.97, 125.42, 123.78, 117.68, 105.78 & 73.58 ppm. Mass (m/z): 335 (M^+ peak).

1c. 2-Benzyloxynaphthalene-1-carbaldehyde: Yield - 76%, M.P. 110 - 112^{o}C, R_f - 0.53 (Ethylacetate :methanol 1:1); IR (KBr) cm^{-1} : 3065(aromatic –CH str),2975(aliphatic –CH str), 1645 (aldehydic -CHO str),1224 (C–O–C str) ;^{1}H NMR($CDCl_3$) ppm: 10.20 (s, 1H, -CHO), 7.99(m, 6H,naph), 6.89 (m, 5H, -$CH_2C_6H_5$), 5.23 (s, 2H, –O–CH_2) ppm;^{13}C NMR ($CDCl_3$) ppm: 192.82, 153.25, 146.59, 134.54, 129.68, 129.52, 128.33, 127.59, 127.47, 126.82, 126.62, 125.64, 125.46, 122.09, 121.82, 121.59, 105.63 & 71.41 ppm. Mass (m/z): 261(M^+ peak).

1d. 2-(4-Nitrobenzyloxy) naphthalene-1-carbaldehyde:Yield - 77%, M.P. 171 - 172 ^{o}C, R_f- 0.57(Ethylacetate: methanol 1:1); IR (KBr) cm^{-1} : 3035(aromatic –CH str),2828(aliphatic –CH str), 1651(aldehydic -CHO str),1225 (C–O–C str) & 816(-NO_2 str);^{1}H NMR ($CDCl_3$) ppm: 10.30 (s, 1H, -CHO), 8.05(m, 6H,naph), 7.28 (m, 4H, -$COCH_2C_6H_4NO_2$-*p*), 5.40 (s, 2H, –O–CH_2) ppm;^{13}C NMR ($CDCl_3$) ppm:): 196.52, 155.25, 138.59, 135.54, 134.03, 130.68, 128.82, 128.33, 127.59, 127.47, 126.92,126.48, 125.64, 125.46, 122.09, 121.82, 103.63 &71.81 ppm.Mass(m/z): 307 (M^+ peak).

2a. 2-(1-Bromonaphthalen-2-yloxy)-1-phenylethanone:Yield - 79%, M.P. 105 - 107 ^{o}C, R_f- 0.53 (Ethylacetate:methanol 1:1): IR (KBr) cm^{-1}: 3048(aromatic –CH str),2968(aliphatic –CH str), 1693 (C=O str), (C–O–C str) & 593(-C-Br str);^{1}H NMR($CDCl_3$) ppm: 8.29(m, 6H,naph), 7.19 (m, 5H, -$COCH_2C_6H_5$), 5.40 (s, 2H, –O–CH_2) ppm;^{13}C NMR ($CDCl_3$) 194.25, 152.68, 134.46, 133.97, 133.22, 130.44, 129.18, 128.98, 128.55, 128.32, 128.06, 127.83, 126.43, 125.80, 124.88, 115,45, 110.27 & 72.86 ppm; Mass(m/z): 341 (M^+ peak).

2b. 2- (1-Bromonaphthalen-2-yloxy) -1- (4-nitrophenyl) ethanone:Yield - 70%,M.P. 108 - 112^{o}C,R_f. 0.48 (Ethylacetate:methanol 1:1);IR(KBr) cm^{-1}:3028(aromatic–CH str), 2982(aliphatic –CH str), 1705(C=O str),1268 (C–O–C str) & 810(-C-N str);^{1}H NMR($CDCl_3$) ppm:8.39(m, 6H,naph), 7.20 (m, 4H, -$COCH_2C_6H_5NO_2$-*p*), 5.52 (s, 2H, –O–CH_2) ppm;^{13}C NMR ($CDCl_3$) ppm: 195.25, 153.68, 136.64, 135.59, 134.28, 131.63, 130.08, 129.58, 129.05, 128.85, 128.46, 128.12, 127.73, 126.80, 125.88, 117.35, 112.18 & 73.52 ppm: Mass(m/z): 381 (M^+ peak).

2c. 2-Benzyloxy-1-bromonaphthalene: Yield-80%,M.P. 95-97 ^{o}C, R_f-0.58 (Ethylacetate: methanol 1:1); IR (KBr) cm^{-1}: 3079(aromatic –CH str),2922(aliphatic –CH str), 1243 (C–O–C str) & 539 (-C-Br str);^{1}H NMR($CDCl_3$) ppm: 8.27(m, 6H,naph), 7.25 (m, 5H, -$CH_2C_6H_5$), 5.30 (s, 2H, –O–CH_2); ^{13}CNMR ($CDCl_3$) ppm: 153.03, 136.74, 133.25, 130.12, 128.82, 128.61, 128.03, 128.01, 127.68, 127.21, 127.18, 126.33, 124.55, 120.01, 115.72, 110.12 & 71.60 ; Mass (m/z): 381 (M^+ peak).

2d. 1-Bromo-2-(4-nitrobenzyloxy) naphthalene: Yield - 70%, M.P. 135-137^{o}C,R_f- 0.55 (Ethylacetate: methanol 1:1); IR (KBr) cm^{-1} : 3085(aromatic –CH str), 2900 (aliphatic –CH str), 1271 (C–O–C str) , 855(-NO_2 str) & 530 (-C-Br str) ;^{1}H NMR($CDCl_3$) ppm: 8.31(m, 6H,naph), 7.15 (m, 4H, -$CH_2C_6H_5NO_2$-*p*), 5.41 (s, 2H, –O–CH_2); ^{13}CNMR

($CDCl_3$) ppm: 152.35, 147.69, 144.06, 133.19, 130.32, 129.12, 128.10, 127.99, 127.55, 126.37, 125.70, 125.52, 124.95, 123.88, 115.16, 110.29 & 71.91; Mass(m/z): 381 (M^+ peak).

Reaction of substituted naphthol(s) with benzyl/phenacyl bromides in presence of micellar medium gave naphthyl ethers. Formation of naphthyl ether was confirmed by the appearance of IR band in the region 1220 cm^{-1} indicating C–O–C ether linkage in the compounds (1a - 1d) and (2a - 2d). Phenacyl / benzyl naphthyl ether(s) show this band[11] at 1200 - 1268 cm^{-1}. For the compounds 1b, 1d, 2b & 2d. This frequency appears at 1224 - 1271 cm^{-1}. This slight increase may be due to the presence of electron withdrawing $–NO_2$ group at para position of benzene ring. The absorption frequency of C=O group of phenacyl ether(s), 1a, 1b, 2a & 2b occurs at 1693 - 1720 cm^{-1}. This observed value is less than that of the saturated aliphatic ketone and this decrease may be due to the conjugation of carbonyl group with aromatic ring which lengthens the C=O bond,. The absorption frequency of aldehydic carbonyl carbon occurs at 1645 - 1653 cm^{-1}. The –C–Br stretching vibration appears at 530 - 586 cm^{-1}.

The ^1H NMR spectrum showed a singlet at 5.68-5.23 ppm due to methylene proton ($–CH_2–O$) of napthyl ether. The other chemical shift values are found to be comparable to the reported values of similar compounds. The $–CH_2–O$ signal moves further to down field 5.81 ppm for the compound 2d. This may be due to the presence of electron withdrawing NO_2 group at *para*-position of benzene ring. Similarly ^{13}C NMR spectra showed a signal at 73.58 ppm due to $–O–CH_2$ of phenacylether. The physical data of the compound 1a - 1d and 2a-2d are summarized in Tables 1 & 2. Mass spectra of the compounds gave the molecular mass of the compounds prepared.

Antimicrobial activity

The compounds (1a - 1d) and (2a - 2d) were screened for their antibacterial activity against *Bacillus cereus, Staphylocus aureus, Aeromonas hydrophila, Proteus mirabilis* and *Aspergillus flaves* and the antifungal activity against *Aspergillus niger* at a concentration of 60 µg/ml of DMSO by Agar-well diffusion method, zone of inhibition in mm.[12-13] Standard antibacterial and anti-fungal drug Gentamycin and Miconozole respectively were also tested under similar conditions for comparison. The results are given in Table-3.

CONCLUSION

A series of substituted naphthyl ethers (1a - 1d) and (2a - 2d) have been newly synthesised and the structures confirmed by spectral analysis. Most of the synthesized compounds have shown antibacterial and antifungal activity to some extent. Among the compounds 1a, 1b, 1d, 2a, 2b and 2d show significant activity while rest show feeble activity against *B. cereus* and *S. aureus.* However, the compounds 1a, 2a and 2d show significant activity against *P. mirabilis.* Compounds 1d & 2b show moderate activity against the same. Others show feeble activities. The compounds 1a, 1b & 2d show significant activity while the 1c, 1d & 2b show moderate activity against *A. flaves*. The compounds 1a & 1b show significant activity, while compounds 1c & 2d show moderate activity against *A. niger*.

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