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Facile Synthesis of Substituted N-Monoalkylaromatic Amines Under PTC Conditions

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FACILE SYNTHESIS OF SUBSTITUTED N-MONOALKYLAROMATIC AMINES UNDER PTC CONDITIONS⁺.

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Abstract: Substituted aromatic amides were alkylated under PTC conditions. Compounds with <u>ortho</u> electron withdrawing substituents furnished exclusively monoalkyl amines. A plausible mechanism has been suggested.

Primary aromatic amines cannot be monoalkylated in satisfactory yields under either normal or PTC condition due to difficulty in removing the NH proton from these amines $(pK_a \text{ aniline } 27^1)$. This difficulty has been overcome by converting the amines to amides, thus facilitating the proton removal and hence the alkylation. We have reported a simple method for the monoalkylation of benzanilides² and diphenylureas³ under PTC conditions. However, in order to get the alkyl amines alkyl amides must be hydrolyzed in a separate these step. A direct conversion of substituted amides to monoalkyl amines is reported; however, it involves

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⁺ NC1 Communication No. 5070.

either the use of costly reagents and solvents⁴ or it does not have general applicability⁵.

In this communication we describe a simple economical one pot synthesis of <u>ortho</u> substituted aromatic monoalkyl amines from corresponding amides/amines using PTC conditions where the substituent is electron withdrawing. The effects of other substituents at the <u>meta</u> and <u>para</u> positions are also discussed. A plausible mechanism is suggested to accommodate the experimental observations.

1-Acetamido or benzamidoanthraquinone (1a,b) and 2-nitroacetanilide or 2-nitrobenzanilide (<u>7</u>n,o) on treatment with dimethyl sulphate, powdered sodium hydroxide and potassium carbonate yielded 1-N-methylaminoanthraquinone (3) and <u>o</u>-nitro-N-methylaniline ($\underline{\mathbf{8n}}$) in quantitative yields. It is quite obvious that these amides were alkylated and deacylated in one pot reacmainly because of the presence of the ortho tion substituents, since the corresponding unsubstituted compounds (**7a**,**b**) furnished only methylated amides (**8a**,**b**) under identical reaction conditions. So in order toascertain the exact role of these substituents in the alkylation and deacylation reactions, alkylation of various substituted aromatic amides (1a,b;5a,b;7a-w) was studied and the results are presented in Tables 1 and 2.

				Table 1	1	
		Methylation	ofa	Methylation of amidoanthraquinone (la.b & 5a.b) using PTC	e (1a.b & 5a.b)	using PTC
5 N	Substrate	UNG		Product	Isolated	M.P/B.P ⁰ C
No	ж	chu mol.	No.	R	% yieta	UDSErved (Literature)
1a	1a coch ₃	1.1	B	Н	9 <i>6</i>	169-70 (170 ⁷)
वा	1b coc ₆ H5	1.1	coj	Н	95	$169-70 \ (170^7)$
वा	1b coc ₆ H5	-	वा	coc ₆ H5	no reaction	
2a	cocH ₃	1	2a	соснз	no reaction	
5a	5a coch ₃	1.1	6a	соснз	95	160-61 C
<u>5</u> b	coc ₆ H5	1.1	<u>6b</u>	coc ₆ H5	93	171-2 C
Rea Vel: C:	ction temp. y. In all y Charecteria	erature and t the reactions sed by elemen	tet ital	for all the react rabutylammonium h and spectral ana.	tions is 30-35 ⁰ C nydrogen sulphat lysis (Table 3).	Reaction temperature and time for all the reactions is 30-35 ⁰ C and 2 hours respectively. In all the reactions tetrabutylammonium hydrogen sulphate is used as PTC. Charecterised by elemental and spectral analysis (Table 3).

AROMATIC AMINES UNDER PTC CONDITIONS

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TABLE 2

Methylation of amides($\underline{\mathbf{Za}}$) in presence of PTC

							and the second	
Sub⊧	strate		Pr(Product		Isolated	M.P/B	M.P/B.P ⁰ C
	Substitu	lent		Substituent	tuent	% yield	Observed Literature	terature
No	ы	R'	No	R	R'			
Ta	Ta coch ₃ H	H	Ba	cocH ₃	Н	98	102	1028
Δī	COC ₆ H5	Н	<u>8</u> b	COC ₆ H5	Н	95	60	60 ⁸
Ζc	cocH ₃	2-C1	Bc	cocH ₃	2-C1	96	125-30/12mm 130/12mm ⁹	130/12mm ⁹
ΡZ	coc ₆ H5	2-C1	Bd	coc ₆ H5	2-C1	96	64	642
Zе	coc ₆ H5	3-C1	ße	coc ₆ H5	3-C1	98	46	462
Ζ£	coc ₆ H5	4-C1	Β£	COC ₆ H5	4-C1	98	68	6910
Ζg	cocH ₃	$2,6-C1_{2}$	<u>8</u> g	cocH ₃	$2, 6-C1_2$	98	66	c
47	COC ₆ H5	2,6-C1 ₂	ßh	COC ₆ H5	2,6-C1 ₂	92	116	U
11	cocH ₃	2,6-(CH ₃) ₂	<u>8i</u>	COCH ₃	2,6-(CH ₃) ₂	98	92	U
Zi	cocH ₃	2,6-(C ₂ H ₅) ₂	<u> </u>	COCH ₃	2,6-(C ₂ H ₅) ₂	96	135-40/3mm	υ
Zk	COC ₆ H5	2-0CH ₃	ßk	COCH ₃	2-0CH3	90	80	802
1	coc ₆ H5	3-0CH3	81	cocH ₃	3-0CH ₃	95	55	5611
Ш	coc ₆ H5	4-0CH ₃	<u>Bm</u>	cocH ₃	4-0CH3	92	73	7610

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Sube	Substrate		Proc	Product	[Isolated		M.P/B.P ⁰ C
	Substitu	uent		Substituent		% yield	Observed	Literature
No	ы	R'	No	R	R'			
Zn	cocH ₃	2-NO2 B	Bn F	Н	2-NO2	98	37	378
ΔĮ	COC ₆ H5	2-NO2 B	BnF	Н	2~NO2	98	37	378
<u>a</u> 7	cocH ₃	4-NO2 8	<u>8</u>	cocH ₃	4-NO2	90	153	15312
Zα	COC ₆ H5	4-NO2 B	B <u>a</u>	coc ₆ H5	4-NO2	95	111	1128
<u>7</u> r	cocH ₃	2-coc ₆ H ₅ B	Br	Н	2-COC ₆ H5	98	68	6913
IB	COC ₆ H5	2-C0C ₆ H ₅ B	Br	Н	2-COC ₆ H5	96	69	6913
Zt	cocH ₃	4-COC ₆ H ₅ B	Bt.	cocH ₃	4-COC ₆ H5	96	106	υ
<u>Zu</u>	COC ₆ H5	4-COC ₆ H ₅ B	Bu	coc ₆ H5	4-COC ₆ H5	95	101	U
74	cocH ₃	2-COC ₆ H5-5-C1 B	<u>8v</u>	Н	2-COC ₆ H ₅ -5-C1	98	95	968
Ţ₩	coc ₆ H5	2-COC ₆ H5-5-C1 BV		Н	2-coc ₆ H ₅ -5-c1	97	96	968
						5		
Read	ction te	Reaction temperature and time for all the reactions is 30-350° and 2 hours respec-	ne fc	ווב תנ	the reactions i	a 30-350	d C pue C	

ы. 1 respec-PTC. In all the reactions, dimethyl sulphate (DMS) 1.05 mole/1.0 mol of amide ខ hours as methylating agent and tetrabutylammonium hydrogen sulphate is used temperature and time for all the reactions is $30-35^{10}$ and 2э). C: Charecterised by elemental and spectral analysis (Table DEACETON tively. nsed

The major conclusions that can be drawn from the observations presented in Tables 1 and 2 may be summarized as follows.

1. Compounds having no substitutents (**7**a,b) yielded only alkyl amides (**8**a,b).

2. Compounds having ortho electron donating substituents ($\underline{\mathbf{7c}}, \mathbf{d}, \mathbf{k}$) also furnished alkyl amides ($\underline{\mathbf{8c}}, \mathbf{d}, \mathbf{k}$).

3. Compounds having ortho substitution with electron withdrawing groups (1a,b;7n,o,r,s,v,w) gave exclusively monoalkyl amines (3,8n,r,v).

4. para-substituents do not have any marked effect on the product pattern. However, compounds having para electron withdrawing substituents (**7p,q,t,u**) furnished mainly alkyl amides (**8p,q,t,u**).

5. meta substituents (7e,1) do not alter the course of the reaction and thus furnish alkyl amides (Be,1).

6. Bulk of the substituents (i.e. chlorine) (**7g**) does not seem to accelerate the deacylation as anticipated. However, this non-accelerataion could be ascribed partly to the electron donating capacity of the chlorine atom.

It was essential to determine the chronology of the reactions, alkylation and deacylation: (a) The deacylation takes place only after alkylation. (b) In the absence of PTC N-alkylacetamido anthraquinone (2a) did not deacylate to give the corresponding alkyl amine (3) thus establishing the essentiality of PTC even for the deacylation step.

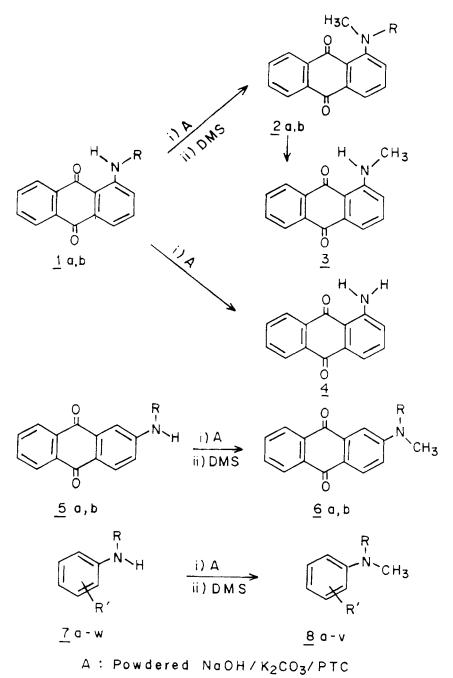
c) Under the reaction conditions the N-alkylated amide could not be isolated or its presence detected by TLC.

Taking into consideration the above phenomena i.e. chronology of reactions, essentiality of PTC and effect of various substituents, a plausible mechanism accommodating all these factor may be depicted as shown in Scheme 2.

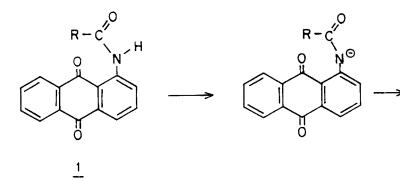
The proposed mechanism was verified⁶ experimentally by alkylation of 1-amino anthraquinone and 1,4diamino anthraquinone to monoalkyl aminoanthraquinones using various alkylating agents in excellent yields.

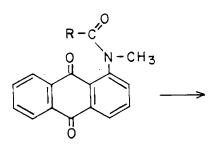
EXPERIMENTAL

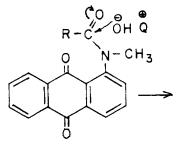
All the melting points/boiling points are uncorrected. Infra red spectra were recorded on Perkin Elmer 137 B in nujol mull in cm^{-1} . ¹HNMR were recorded on Brucker W.H.-90 FT spectrometer using TMS as internal standard. Mass spectra were scanned on CEC-21-110 B machine. Purity of the compounds were checked by TLC. All the new compounds gave satisfactory elemental analysis. All the substrates were either procured from market or prepared following established procedures.

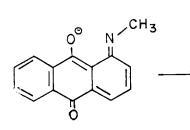


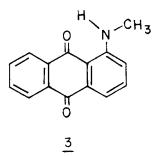
Scheme 1











 $R = COCH_3$, COC_6H_5



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Table 3

Spectral and elemental analysis of N-monoalkylanilides($\underline{6}a, b$ and $\underline{8}g-j, t, u$)

Comp M ⁺ No. ion	M+ ion	IR C=0 cm ⁻¹	1HNMR (CDC13) Chemical shift in (6) PPM	Molecular formula	Elemen Found C	Elemental analysis% Found (calculated) C H N	ysis% ted)
Ga	279	1640	1.94(s, 3H), 3.31(s, 3H) 7.50-7.87(m, 3H), 8.0-8.37	C17H13N03	73.25 (73.11)	4.96 (4.65)	5.15 (5.01)
<u>6</u> b		1635	(m, 4n) 3.59(s, 3H), 7.0-746(m, 5H) 7.62-7.82(m, 3H), 8.13-8.34 (m 4H)	$C_{22}H_{15}NO_{3}$	77.34 (77.71)	4.67 (4.31)	4.55 (4.10)
<u>8</u> g		1680	(m, T.) 1.7(s, 3H), 3.1(s, 3H) 7.17-7 53(m 3H)	c9H9C12NO	50.26 (49.54)	4.16	6.20 (6.42)
ßh		1650	3.17(s, 3H), 6.63-7.26 (m, 8H)	$C_{14}H_{11}C1_{2}NO$	60.05 60.05	3.85 3.85	5.10 5.10
<u>8i</u>		1660	ан, сл., 1.46(s, ЗН), 2.23(s, 6Н) З Оба ЗН) 7 1(в ЗН)	$C_{11}H_{15}NO$	74.32	(8.47) (8.47)	7.86
8.	205	1660	1.50(m, 6H), 1.83(s, 3H) 2.70(g, 4H), 3.23(s, 3H) 7.06.7 3(m, 3H)	C13H19NO	(76.09) (76.09)	9.26) (9.26)	(6.83)
Bt	253	1640	2.04(s, 3H), 3.37(s, 3H) 7.22.4(s, 11(m, 9H)	$c_{16}H_{15}NO_{2}$	75.41	5.95 (5.95	5.36 (5.53)
Bu	315	1630		$C_{21}H_{17}NO_{2}$	(80.00) (80.00)	(5.93)	(2, 20) 4, 50) (4, 44)

General procedure for N-alkylation of aromatic amides. N-Methylation of 1-benzamido anthraguinone (1b)

a three necked round bottom flask, mixture of In (0.02)mol) powdered sodium hydroxide (0.08 mol), 1bpowdered anhydrous potassium carbonate (0.2 mol) and tetrabutylammonium hydrogen sulphate (0.0004 mol) was stirred in toluene (100 ml) for 30 minutes at $30-35^{0}$ C. Reaction mixture was deep yellow initially became deep violet and slimy mass was seen sticking to the walls of flask. Freshly distilled dimethyl sulphate (0.021 the mol) diluted with toluene 10 ml was slowly added to the reaction mixture over a period of 30 minutes. As addition proceeded, deep violet color turned in to deep red (reaction was monitored by TIC). The reaction mixture stirred at 30-35 °C for 1 h, filtered and washed was with toluene (3 x 25 ml). Toluene main filtrate and washings were combined, washed with water (2 x 50 ml), dried over anhydrous sodium sulphate and concentrated to yield colored solid product, which was characterized as 1-N-methylamino anthraquinone 3(4.5 g., 0.019 mol, 95%) m.p. 169-70°C (Lit. 170¹³).

Similarly 1a, 5ab and 7a-w were methylated under identical conditions and results are tabulated in Table 1 and 2. Elemental analysis and spectral data for new compounds are given in Table 3

REFERENCES

- Dehmlow, E.V., Thieser, R., Zahalka, H.A., and Sasson, Y. Tet. Lett., 1985, <u>26</u>, 297-300.
- Ayyangar, N.R., Choudhary, A.R., Kalkote, U.R. and Natu, A.A. Synth. Communication, 1988, <u>18</u>, 2011-2016.
- Ayyangar, N.R., Choudhary, A.R., Kalkote, U.R. and Natu, A.A. Chemistry & Industry, 1988, 599-600.
- 4. Mouzin, G., Cousse, H. and Autin, Jean-Marie, Synthesis, 1981, 448.
- Sharma, V.K, Kumar, A. and Agarwal, P.K. Ind. J. Chem., 1983, <u>22</u>, 1153.
- Kalkote, U.R., Choudhary, A.R., Natu, A.A. and Ayyangar, N.R. Synthetic Communication (in press).
- 7. Wilson, C.V., Dickey, J.B. and Allen, C.F.H. Organic Synthesis, 1949, <u>29</u>, 66-68.
- Dictionary of organic compounds, Chapman and Hall, New York, London 5th edition.
- 9. Huisgen, R., Bayerlein, F. and Heydkamp, W. Chem. Ber., 1959, <u>92</u>, 3223-3241; C.A. 1960, <u>54</u>, 6595a.
- Fox, B.L. and Doll, R.J. J. Org. Chem., 1973, <u>38</u>, 1136-1140.
- Bevis, M.J., Forbes, E.J., Naik, N.N. and Uff, B.S. Tetrahedron, 1971,<u>27</u>, 1253-1259.
- 12. Morgan, G.T. and Grist, W.R., J. Chem. Soc., 1918, 691.
- 13. Bielstein, XIV, I, 387.

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