Pakistan J. Sci. Ind. Res. Vol. 27, No. 6, December 1984.

TRANSALKYLATION AND TRANSARYLATION OF QUATERNARY PYRIDINIUM SALTS

— Conversion of Primary Amines into Alkyl and Aryl Bromides

Sayed M.M. Elshafie

Chemistry Department, Faculty of Sciences, Minia University, Minia, Egypt.

(Received September 21, 1982; revised September 16, 1984).

Primary alkyl, aryl, and heteroaryl amines are converted both by tricyclic and pentacyclic pyrylium bromides into the corresponding tricyclic and pentacyclic pyrindinium bromides in good yields. The latter when subjected to solvolysis by refluxing in 1,4-dioxane gave the required alkyl, aryl, and heteroaryl bromides.

INTRODUCTION

Comparing the traditional routes for the conversion of aminoarenes into halides via the diazonium function [1], there are few comparable transformations in the aliphatic series. One extensively studied conversion of primary and secondary alkyl amines to chlorides and bromides is the von Braun method [2] of acylation of the amine to an amide which is subsequently treated with phosphorus penthalide [3, 4] or thionyl chloride [5].

Yields are generally 50-70% for the von Braun reaction, but the disadvantages of the method include the drastic conditions and its limitations to compounds which do not have boiling points near those of either the phosphorus oxychloride or the benzonitrile. Other conversions of tertiary amines into alkyl bromides involve their reaction with cyanogen bromide [6] or hydrogen bromide [7]. The generality and synthetic utility of these methods are limited. More recently [8] primary amines have been converted by an arenediazonium salt into a triazene which on treatment with aqueous hydrogen bromide gives the bromide (eq. 1). The overall yields are *ca.* 60% but side reactions lead to olefines and secondary amines.

$$RNH_2 \xrightarrow{Ar\text{-}N_2^+} RNH\text{-}N{=}N\text{-}Ar \xrightarrow{HBr} R\text{-}Br \quad (1)$$

Alkylamines have also been converted into arylsulphonamides [9] which on reaction with potassium bromide or iodide in dimethylformamide give alkyl halides.

Now this reported work in the transalkylation, transarylation and transheteroarylation of N-substituted-5, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b] pyridinium bromides **4** a-d and N-substituted-5, 6, 8, 9-tetrahydro-7-phenyldibenzo [c, h] acridinium bromides **8** a-e were useful in the synthesis of alkyl, aryl and heteroaryl bromides. This novel method for the preparation of the above mentioned bromides from primary amines could be attributed to the sufficient steric hindrance of the tricyclic and pentacyclic pyridinium cations in a new two-step process. The main point is the novel pyridinium system [10], the *N*-substituted-5, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b] pyridinium bromides **4** a-d, were prepared by mixing 5, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b]-pyrylium bromide **3** and the appropriate amine in methanol. The pyrylium cation **1** could be prepared by condensation of 2-benzyliden-1-tetralone with acetophenone in the presence of etherated solution of boron trifluoride. Compound **1** was isolated in 60% yield and then converted into pseudobase **2** by heating under reflux in an ethanol solution of sodium hydroxide then converted into the pyrylium bromide 3 by refluxing with hydrogen bromide ethanol mixture (Chart 1, Table 1).

Also N-substituted 5, 6, 8, 9-tetrahydro-7-phenyldibenzo [c, h] acridinium bromides 8 a-e were prepared by refluxing 5, 6, 8, 9-tetrahydro-7-phenyldibenzo [c, h] xanthylium bromide **7** and the appropriate amine in dimethylformamide. The xanthylium tetrafluoroborate 5 was isolated in 70% yield by the interaction of 2-benzylidene-α-tetralone with 1-tetralone in the presence of boron trifluoride etherate. The obtained product **5** was transformed into the pseudo-base by refluxing in ethanolic solution of sodium hydroxide, then treating the obtained pseudobase **6** with HBr ethanol mixture to obtain xanthylium bromide **7** (Chart 2, Table 2).

The characteristic spectral details of these N-substituted pyridinium cations **4** a-d and acridinium cations **8**

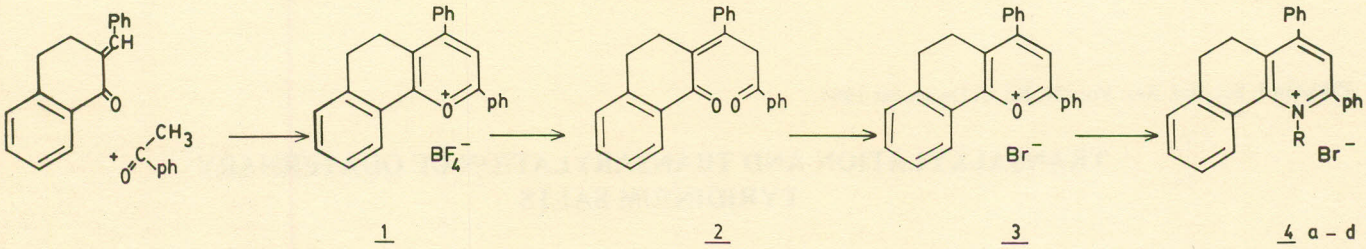

Chart 1

Table 1. Physical and analytical data of N-substituted-5, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b] pyridinium bromides **4** a-d.

N-Substituent	Yield %	M.P. °C	Formula	Found C	H	N	Br	Required % C	H	N	Br
4a Phenyl	84	230	$C_{31}H_{24}BrN$	75.7	4.9	3.1	16.0	75.9	4.9	2.9	16.3
4b 3-Methylphenul	88	200	$C_{32}H_{26}BrN$	76.4	5.2	2.9	16.1	76.2	5.2	2.8	15.9
4c 4-Methylphenyl	92	271	$C_{32}H_{26}BrN$	76.6	5.0	3.0	15.6	76.2	5.2	2.8	15.9
4d 2-Pyridyl	95	280	$C_{30}H_{23}BrN_2$	73.6	4.6	5.4	16.0	73.3	4.7	5.7	16.3

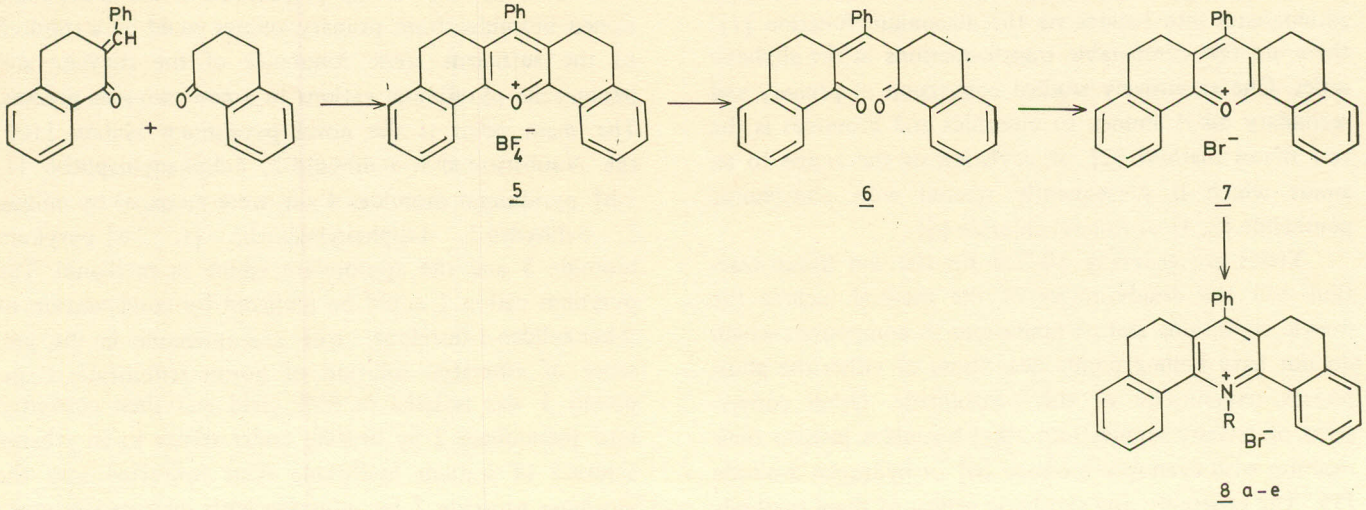

Chart 2

Table - 2. Physical and analytical data of N-substituted-5, 6, 8, 9-tetrahydro-7-phenyldibenzo [c, h]] acridinium bromides **8** a-e.

N-substituent	Yield %	M.P. °C	Formula	Found C	H	N	Br	Required % C	H	N	Br
8a Methyl	60	155	$C_{28}H_{24}BrN$	73.8	5.4	3.1	17.5	74.0	5.3	3.1	17.6
8b Phenyl	56	292	$C_{33}H_{26}BrN$	76.5	5.3	2.7	14.3	76.7	5.0	2.7	14.5
8c 3-Methylphenyl	55	294	$C_{34}H_{28}BrN$	77.2	5.0	2.6	15.5	77.0	5.3	2.6	15.1
8d 4-Methylphenyl	67	305	$C_{34}H_{28}BrN$	77.4	5.3	2.7	15.0	77.0	5.3	2.6	15.1
8e 4-Methoxyphenyl	71	297	$C_{34}H_{28}BrNO$	74.3	5.0	2.7	14.2	74.7	5.1	2.6	14.7

a-e are listed in Table 3. The IR spectra of the pyridinium salts **4** a-d and acridinium salts **8** a-e show the typical pyridinium bands and acridinium bands at 1613-1600 cm^{-1} and 1599-1590cm^{-1} as also the typical band for the bromonium anion at 1250-1170 cm^{-1}. The *N*-substituted pyridinium compounds **4** a-d and acridiniums **8** a-e when refluxed in 1,4-dioxane for 10 hr with stirring gave the corresponding bromo-derivatives (Table 3) in 51-82% yield. It was noticed that the yield of bromo-derivatives obtained by the solvolysis of N-substituted-5, 6, 8, 9-tetrahydro-7-phenyldibenzo [c, h] acridinium bromides were higher than that obtained from **N-substituted-5**, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b] pyridinium bromides also the time of reaction is less in case of the former **8** due to high steric effect and hence ease of solvolysis.

1-tetralone (2) separated out (16.4g, 100%); it was crystallised from absolute ethanol as plates, m.p. 139°C (Found: C, 85.1; H, 5.3 $C_{25}H_{20}O_2$ requires: C, 85.2; H, 5.7%); δ [DMSO d_6] 8.2-7.8 (4H, m, aromatic protons), 7.8-7.2 (10H,m, aromatic protons), 3.5 (2H,s,-CH_2), 3.1 - 2.7 (2H,m,-CH_2), 2.7-2.4 (2H,m,-CH_2).

γ_{max} (Nujol) 1675, 1650, 1325, 1318, 1292, 1245, 1220, 1179, 1153, 1020, 1000, 965, 932, 909, 805, 765, 745, 738, 718, 705 and 685 cm^{-1}.

Preparation of 5, 6-dihydro-2, 4-diphenylnaphtho [1, 2-b] pyrylium bromide **(3)**.– A solution of pseudo-base **(2)** (20g, 0.06 mol) in ethanol (100 ml) was heated to reflux. Concentrated hydrobromic acid was added (6.2g, 0.08 mol) and heating continued for 0.5 hr.

Table 3. PMR-spectra (60 MHz) of pyridinium bromides **4** a-d, and acridinium bromides **8** a-e.

Compd.*	Aromatic protons (δ)	$(-CH_2CH_2-)^n$	Alkyl protons
		n = 1	
4a	7.9-6.8 (19H,m), 6.8-6.5 (1H,d)	2.9 (4H,5)	
4b	7.8-6.8 (18H,m), 6.8-6.5 (1H,d)	2.9 (4H,s)	2.5 (3H,s)
4c	7.8-6.8 (18H,m), 6.8-6.5 (1H,d)	2.9 (4H,s)	2.5 (3H,s)
4d	9.0-8.8 (1H,d), 8.7-8.3 (2H,m), 8.2 (1H,s), 7.9-7.0 (14H,m), 7.0-6.7 (1H,d)	3.9-3.0 (4H,m)	
		n = 2	
8a	8.4-8.0 (2H,m) 7.8-7.2 (11H,m)	2.8 (8H,s)	4.6 (3H,s)
8b	7.8-6.8 (16H,m), 6.8-6.6 (2H,d)	2.9 (8H,s)	
8c	7.8-6.7 (15H,m), 6.8-6.5 (2H,d)	2.9 (8H,s)	2.5 (3H.s)
8d	7.8-6.8 (15H,m), 6.7-6.5 (2H,d)	2.9 (8H,s)	2.5 (3H,s)
8e	7.9-6.8 (15H,m), 6.8-6.5 (2H,d)	2.9 (8H,s)	4.0 (3H,s)

* $CH_3CO_2H/CDCl_3$ mixture used as solvent.

EXPERIMENTAL

The IR and NMR-spectra were measured with Perkin-Elmer 237 and R 12 (60 MHz) instruments respectively (TMS as internal standard).

Melting points (uncorrected) were determined by using the Gallenkamp melting point apparatus.

Pseudo-base (2). – 5, 6-Dihydro-2, 4-diphenylnaphtho [1, 2-b] pyrylium tetrafluoroborate (1) (19.8 g, 0.047 mol) was suspended in boiling ethyl alcohol (150 ml) and NaOH (2 g, 0.047 mol) in water (10 ml) was added dropwise until a permanent red colour change was observed. On cooling the 2-(1, 3-diphenyl-3-oxopropylidene)-

The mixture was cooled, then poured into diethyl ether (300 ml) and the product filtered and recrystallised from ethanol to yield the bromide **(3)** (212g, 90%), m.p. 269°C. (Found: C, 72.5; H, 4.3; Br, 19.4; $C_{25}H_{19}BrO$ requires C, 72.3; H, 4.6; Br, 19.3%). δ [dmso d_6], 8.5-8.1 (4H,m,aromatic protons), 7.9-7.3 (11H,m, aromatic protons), 3.5-2.9 (4H, 6m, 2-CH).

IR ($CHBr_3$) 1612 s, 1598 s, 1575 m, 1492 vs, 1472 vs, 1442 s, 1423 s, 1385 m, 1343 w, 1324 w, 1303 w 1280 w, 1245 m, 1215 ms, 1190 w, 1173 m, 998 w 932 w, 875 ms, 822 w, 788 ms, 779 m, 765 ms, 745 s, 730 w, 702 ms, $cm.^{-1}$

Preparation of N-substituted-5, 6-dihydro-2, 4-diphenylnaphtho-[1, 2-b]pyridinium bromides **4** *a-d (Table 1): General Procedure.* – The amine (0.012 mol. was added, dropwise, with stirring at 20° to 5, 6-dihydro-2, 4-diphenyl-naphtho [1, 2-b] pyrylium bromide **3** (0.01 mol) in methanol (50 ml). Stirring was maintained for 2 hr, the solvent was evaporated under reduced pressure, and the residual pyridinium bromide was crystallised from methylene chloride and diethyl ether in the form of white needles (Table 1).

Preparation of pseudo-base (**6**) 5,6,8,9-Tetrahydro-7-phenyldibenzo [c,h] xanthylium tetrafluoroborate (**5**) 10 g, 0.02 mol) was refluxed in ethanol (50 ml); and 6 N sodium hydroxide solution was added dropwise till a permanent violet coloration was obtained. The solution was cooled to 0°C and filtered (8.2 g, 96%). The product was recrystallised from absolute ethanol m.p. 172°C.

Preparation of 5,6,8,9-tetrahydro-7-phenyldibenzo [c,h]- xanthylium bromide (7).The pseudo-base (6) (5.0 g, 0.01 mol) was refluxed in absolute ethanol (40 ml), with hydrobromic acid (1 g, 0.01 mol) for 0.5 hr. On cooling to 30°C the product was poured into diethyl ether (100 ml). This precipitate of the pyrylium salt was filtered, and recrystallised from ethanol, (5.1 g, 89%) as reddish needles, m.p. 292-293°C. (Found: C, 73.2; H,4.5; Br, 18.0, $C_{27}H_{21}BrO$ requires C, 73.5; H, 4.8; Br, 18.1%); [DMSO d_6] 8.5-8.3 (2H,m, aromatic protons), 7.9-7.2 (11 H,m, aromatic protons), 3.0 (8H,s,4-CH_2).

Ir- ($CHBr_3$) γ_{max} 1612s, 1602s, 1563s, 1475s, 1415s, 1400m, 1210 m, 1198 m, 890 m, 803 m, 785 ms, 760 ms, 694 s, $cm.^{-1}$

Preparation of N-methyl-5,6,8,9-tetrahydro-7-phenyldibenzo- [c,h] acridinium bromide (**8a**).– A mixture of xanthylium salt (7) (2.5 g, 0.0056 mol) and methylamine (0.2 g, 0.006 mol) was stirred at room temperature for 3 hr in methanol (20 ml).

The solvent was removed under vacuum and the residue triturated with ether (50 ml). Filtration gave (1.5 g, 60%) of a solid, which on recrystallisation from *iso*propyl alcohol gave (8a) white needles, m.p. 155° (Table 2).

Preparation of N-substituted-5,6,8,9-tetrahydro-7-phenyldibenzo [c,h] acridinium bromides (8 b-e), (Table 2). A mixture of xanthylium salt (7) (2.5 g, 0.0056 mol) was refluxed with the required amine (0.006 mol) in dimethyl-formamide (10 ml) for 3 hr. The solution was then cooled to room temperature and the addition of ether (70 ml) precipitated the product. This was filtered and recrystallised from methylene chloride and ether giving the corresponding pyridinium salts in the form of needles.

General procedure for the preparation of alkyl, aryl, and heteroaryl bromides 9 a-f, (Table 4). The appropriate N-substituted pyridinium bromide **4** a-d or acridinium bromides **8** a-e (10 mmol), was refluxed in 1,4-dioxane (30 ml) for 10 hr; subsequently the volume of the reaction mixture was reduced to 1/3 under reduced pressure and added to water (200 ml). 5,6,8,9-tetrahydro-7-phenyl-dibenzo [c,h] acridine precipitated out, filtered and the bromo-compound was extracted with ether (300 ml), dried by anhydrous $MgSO_4$, followed by fractional distillation of the extract (Table 4, Chart 3).

Table 4. Physical and analytical data of alkyl, aryl and heteroaryl bromides (9 a-f[11]).

Compd.	Products*	Material	Yield %	B.P. °C	M.P. °C	n_D^{20}	d_D^{20}
9a	Methylbromide	8a	60	– 4.6			1.732
9b	Bromobenzene	4a	72	156	– 31	1.558	1.491
		8b	81				
9c	*m*-Bromotoluene	4b	65	183.7	– 40	1.5517	1.410
		8c	79				
9d	*p*-Bromotoluene	4c	63	184	29		1.390
		8d	82				
9c	*p*-Bromoanisol	8e	56	223	10	1.5630	1.494
9f	2-Bromopyridine	4d	51	194		1.5720	1.657

* Identified by comparison with TLC and IR-spectra compared with authentic samples.

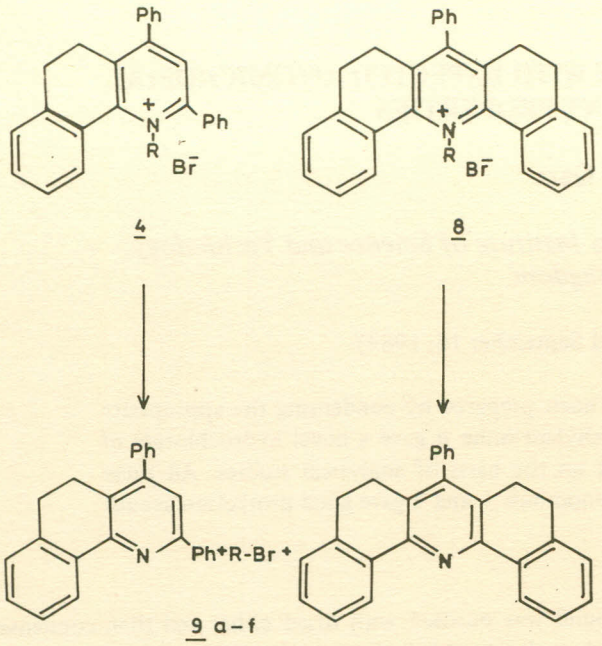

Chart 3

Footnotes. In the preparation of methyl bromide **(9a)** from **(8a)** cooled trape, by liquid nitrogen, was used to collect the product.

The reaction time when utilising the pentacyclic pyridinium salt was shorter than in the case of tricyclic system due to high steric effect.

REFERENCES

1. Houben-Weyl, Methoden der Organischen Chemie, ed. Muller E., Verlag G.T., Stuttgart, Band 5/3 (1962) 846; Band 5/4 (1960), 437.
2. J. von Braun,Chem.Ber., **37** (1904), 2915 and 3210.
3. H.von Pechmann, Chem.Ber., 33(1900) 611; I.von Braun, *Ibid.*, **37**, 2812 (1904).
4. J. von Braun, Org. Synth. Coll., **1**, 428 (1941).
5. J.von Braun and W. Pinkernelle, Chem. Ber., **67**, 1218 (1934)W.R. Vaughan and R.D. Carlson, J. Am. Chem. Soc., **84**, 769 (1962).
6. J. von Braun, Chem Ber, **33**, 1438 (1900).
7. R.A. Chambers and D.E. Pearson., J.Org.Chem., **28**, 3144 (1963).
8. E.H. White and H. Scherrer, Tetrahedron Letters, 758 (1961).
9. P.J. Dechristopher, J.P. Adamek, C.D. Lyon, J.T. Galante, H.E. Haffner, R.J. Boggio, and R.J. Baungarten, J. Am. Chem. Soc., **91**, 2384 (1969).
10. S.M. Elshafie, Indian J.Chem., **20B**, 427 (1981).
11. J.A. Dean *Lange's Hand Book of Chemistry* (1973), eleventh editions.