Synthesis and Hydrolysis of Substituted Tetrahydropyrimidinium Salts. Behaviour of the Degradation Products on Varying *p*H.

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Reaction of 1,2-diaryl-3-methyl-1,4,5,6-tetrahydropyrimidinium iodides **1a-i** with alkaline solutions afforded *N*-aroyl-*N*-aryl-*N'*-methyltrimethylenediamines **2a-i**. Compounds **2** are stable under acid conditions but in neutral or alkaline media spontaneously rearrange giving *N*-aroyl-*N'*-aryl-*N*-methyltrimethylenediamines **3a-i**. Treating compounds **3** with concentrated acids reverse reaction takes place.

Kinetic studies were performed on this intramolecular N → N' aroyl transfer over the H_o-*p*H range -0.9 to 2.30. Compounds **3** undergo acyl transfer to give **2** by a mechanism which involves a change in the rate determining step from formation to acid-catalysed decomposition of a six-membered heterocyclic intermediate on going from H_o to *p*H values. The existence of maxima in the *p*H rate profile allow to determine apparent p*K*a values of the hexahydropyrimidine intermediates which gave good correlation with the Swain *F* substituent constants. Stability of these heterocycles was also predicted by determination of thermodinamic parameters. Comparisons are made with the behaviour of five-membered heterocyclic intermediates (imidazolidine derivatives) which were studied in an earlier paper.

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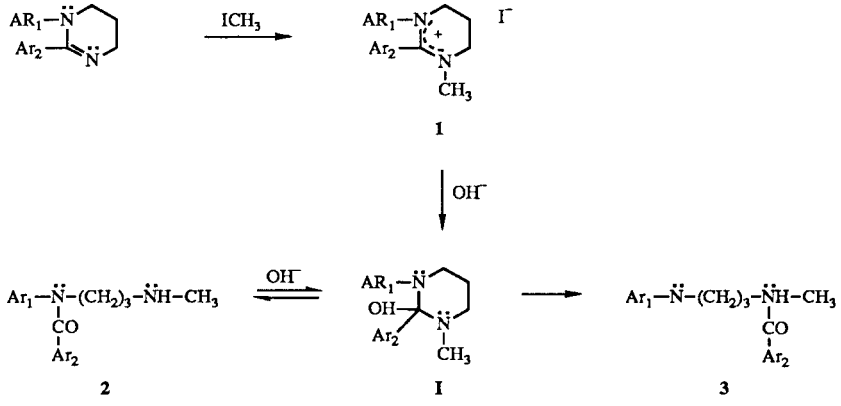
Continuing our study on the reactions of asymmetric cyclic amidinium compounds with nucleophiles [1-4], we have examined the alkaline hydrolysis of 1,2-diaryl-3-methyl-1,4,5,6-tetrahydropyrimidinium iodides **1a-i**.

Here is also reported the behaviour of their degradation products on varying *p*H in order to compare our results with those obtained from imidazolinium salts [4].

Compounds **1** were synthesized by treatment of the corresponding 1,2-diaryl-1,4,5,6-tetrahydropyrimidine with methyl iodide in methylene chloride solution. Treatment of an aqueous solution of **1** with cooled 30% sodium hydroxide afforded *N*-aroyl-*N*-aryl-*N'*-methyltrimethylenediamine **2** by a kinetically controlled reaction. Compounds **2** are stable under acid conditions but in neutral or alkaline media spontaneously rearrange giving *N*-aroyl-*N'*-aryl-*N*-methyltrimethylenediamines **3** by aroyl transfer (Scheme I). An intermediate of this reaction, presumably the pseudobase **I** was detected by hptlc. The presence of an intermediate having similar chromatographic characteristics as **I** was detected when **1** was treated with diluted

Scheme I

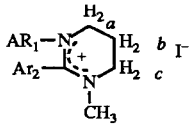


1 **2** **I** **3**

1,2,3	Ar_1	Ar_2
a	C_6H_5	C_6H_5
b	*p*-$NO_2C_6H_4$	C_6H_5
c	*p*-$CH_3OC_6H_4$	C_6H_5
d	*p*-ClC_6H_4	C_6H_5
e	*p*-$CH_3C_6H_4$	C_6H_5
f	β-$C_{10}H_7$	C_6H_5
g	C_6H_5	*p*-$NO_2C_6H_4$
h	C_6H_5	*p*-$CH_3OC_6H_4$
i	C_6H_5	*p*-ClC_6H_4

Table I

1,2-Diaryl-3-methyl-1,4,5,6-tetrahydropyrimidinium Iodides **1b-i**



Compound No.	Yield %	MP °C	Analyses Calcd./Found %C	%H	%N	IR ν(cm^{-1})		^{1}H NMR δ (ppm)	Multi-plicity	Assignment	^{13}C NMR δ (ppm)	Assignment [a]
1b	84	180	48.23	4.25	9.93	2900 (w)	(C-H)	7.80-7.35	m	aromatics	19.27	CH_2 b
			48.16	4.29	9.88	1620 (m)	amidinium	7.10-6.85	m	CH_5-C≡ (3, *meta* and *para* H)	42.57	CH_3
						1350 (m)	(C-N)	4.1	[b]	CH_2 *a* and *c*	48.56-50.07	CH_2 *a* and *c*
						1320 (s)	(NO_2)	3.1	s	N-CH_3	124.0-127.17	aromatics
						1300 (s)	(C-N)	2.6	Q	CH_2 *b*	128.6-128.87	
						850 (s)	(p-C_6H_4)				131.12-146.17	
						690 (s)	(C_6H_5)				147.13-149.69	
											162.15	C_2
1c	79	216	52.94	5.15	6.86	3020 (w)	(C-H)	7.75-7.60	m	CH_5-C≡ (2, *ortho* H)	19.01	CH_2 *b*
			52.90	5.23	6.78	2930 (w)	(C-H)	7.25	d	-C_6H_4-N$^+$≡ (2, *ortho* H)	42.05	CH_3-N
						1600 (m)	amidinium	7.20-7.10	m	CH_5-C≡ (3, *meta* and *para* H)	47.90-49.96	CH_2 *a* and *c*
						1385 (m)	(C-N)	6.5	d	O-C_6H_4 (2, *ortho* H)	54.53	CH_3O-
						1300 (m)	(C-N)	4.05	[c]	CH_2 *a* y *c*	113.39-127.26	aromatics
						1250 (s)	(C-O)	3.70	s	O-CH_3	127.67-127.85	
								3.10	s	N-CH_3	128.26-129.92	
						840 (m)	(p-C_6H_4)	2.60	Q	CH_2 *b*	134.50-157.99	
						705 (m)	(C_6H_5)				162.03	C_2
1d	70	197	49.45	4.37	6.79	3010 (w)	(C-H)	7.75-7.50	m	CH_5-C≡ (2, *ortho* H)	19.00	CH_2 *b*
			49.40	4.48	6.82	1610 (m)	amidinium	7.35	d	C_6H_4-N$^+$≡ (2, *ortho* H)	42.20	CH_3-N
						1380 (m)	(C-N)	7.25-7.00	m	CH_5-C≡ (3, *meta* and *para* H)	48.05-49.85	CH_2 *a* and *c*
						1310 (m)	(C-N)	6.95	d	Cl-C_6H_4 (2, *ortho* H)	127.31-128.10	aromatics
						845 (s)	(p-C_6H_4)	4.00	[b]	CH_2 *a* and *c*	128.41-128.59	
						700 (m)	C_6H_5	2.90	s	N-CH_3	130.36-133.34	
								2.60	Q	CH_2 *b*	140.20	
											161.91	C_2
1e	78	160	55.10	5.36	7.14	2950 (w)	(C-H)	7.60-7.40	m	CH_5-C≡ (2, *ortho* H)	19.27	CH_2 *b*
			55.17	5.44	7.13	1620 (s)	amidinium					
						1595 (s)	(C=C)	7.20-6.90	m	aromatics	20.30	CH_3-Ar
						1380 (m)	(C-N)	6.73	d	C_6H_4-CH_3 (2, *ortho* H)	42.28	CH_3-N
						1310 (s)	(C-N)				48.21-50.02	CH_2 *a* and *c*
						810 (m)	(p-C_6H_4)	4.00	[c]	CH_2 *a* and *c*	126.50-127.78	aromatics
						695 (m)	(C_6H_5)	3.05	s	N-CH_3	128.07-128.57	
								2.50	Q	CH_2 *b*	129.19-130.21	
								2.10	s	C_4H_6-CH_3	137.66-139.37	
											162.09	C_2
1f	83	225	58.88	4.95	6.54	2980 (w)	(C-H)	8.20-7.25	m	aromatics	19.43	CH_2 *b*
			58.80	4.99	6.58	1610 (s)	amidinium	4.15	[b]	CH_2 *a* and *c*	42.41	CH_3-N
						1600 (s)	(C=C)	3.10	s	N-CH_3	48.39-50.23	CH_2 *a* and *c*
						1375 (m)	(C-N)	2.65	Q	CH_2 *b*	124.15-125.94	aromatics
						1305 (s)	(C-N)				126.23-126.46	
						700(m)	(C_6H_5)				126.94-127.41	
											127.73-128.15	
											128.69-128.88	
											130.35-131.57	
											132.18-139.26	
											162.29	C_2

Table I (continued)

Compound No.	Yield %	MP °C	Analyses Calcd./Found %C	%H	%N	IR λ(cm^{-1})	amidinium	^{1}H NMR δ (ppm)	Multi-plicity	Assignment	^{13}C NMR δ (ppm)	Assignment [a]
1g	70	204	48.23	4.25	9.93	2930 (w)	(C-H)	8.30-7.90	m	C_6H_4-NO_2	19.30	CH_2 *b*
			48.26	4.32	9.87	1625 (s)	amidinium	7.60-7.00	m	C_6H_5	41.80	CH_3-N
						1595 (s)	(C=C)	4.30-4.00	m	CH_2 *a* and *c*	48.30-49.88	CH_2 *a* and *c*
						1380 (m)	(C-N)	3.10	s	*N*-CH_3	123.50-127.40	aromatics
						1305 (s)	(C-N)	2.70	Q	CH_2 *b*	127.48-128.04	
						850 (s)	(*p*-C_6H_4)				128.50-128.95	
						700 (s)	(C_6H_5)				141.35-148.10	
											162.10	C_2
1h	78	180	52.94	5.15	6.86	2930 (w)	(C-H)	7.60	d	CH_4-N^+≡	19.30	CH_2 *b*
			53.00	5.23	6.82	1610 (s)	amidinium			(2, *ortho* H)	42.08	CH_3-N
						1595 (s)	(C=C)	7.50-7.00	m	C_6H_5	48.50-50.65	CH_2 *a* and *c*
						1380 (m)	(C-N)	6.74	d	*o*-C_6H_4	54.78	CH_3O
						1260 (s)	(C-O)			(2, *ortho* H)	114.38-124.32	aromatics
						845 (s)	(*p*-C_6H_4)	4.02	m	CH_2 *a* and *c*	127.50-128.05	
						700 (s)	C_6H_5	3.75	s	*O*-CH_3	128.40-129.05	
								3.10	s	*N*-CH_3	141.35-157.04	
								2.60	Q	CH_2 *b*	162.38	C_2
1i	95	238	49.45	4.37	6.80	3010 (w)	(C-H)	7.65	d	CH_4-C^+≡	19.76	CH_2 *b*
			49.30	4.48	6.82	2920 (w)	(C-H)			(2, *ortho* H)	41.56	CH_3-N
						1620 (s)	amidinium	7.50-6.90	m	aromatics	48.20-50.32	CH_2 *a* and *c*
						1595 (s)	(C=C)	4.00	m	CH_2 *a* and *c*	124.30-127.52	aromatics
						1380 (m)	(C-N)	2.90	s	N-CH_3	128.14-128.56	
						1310 (s)	(C-N)	2.40	Q	CH_2 *b*	130.04-134.30	
						840 (s)	(*p*-C_6H_4)				141.09	
						690 (s)	(C_6H_5)				162.10	C_2

[a] The assignment was made on the basis of the analysis of decoupled and coupled spectra and attached proton test (APT). [b] Quintuplet with relation of areas 1:3:2:3:1 by overlap of the triplets. [c] Quadruplet with relation of areas 1:4:4:1 by overlap of the triplets.

sodium hydroxide and before the appearance of compound **2**. Therefore, it is inferred that the pseudobase **I** is a common intermediate of the reactions **1**→**2** and **2**→**3** (Scheme I).

When compounds **3** are treated with aqueous concentrated acids they undergo an acid catalysed rearrangement to **2** showing a similar behaviour as that observed for *N*-alkyl-*N*-aroyl-*N'*-arylethylenediamines [4]. We tried to gain further insight into the mechanism of this reaction which involves the formation and acid catalysed decomposition of a hexahydropyrimidine intermediate **I** which is present under steady state conditions as it was demonstrated by kinetic methods [4].

In fact, reaction **3**→**2** exhibits a *p*H rate maximum (Figure 1) which can be explained by postulating a change in the rate determining step from formation to decomposition of a protonated intermediate **I** as it was analysed for imidazolidine derivatives (Schemes II and III in our previous paper [4]).

Rate constants of transfer are listed in Table IV. They are in general one logarithmic unit lower than those of the five-membered intermediate heterocycles (n = 2) (Table IV) denoting a major stability of the intermediate **I** (n = 3) to the acid hydrolysis.

The appearance of **2** was followed by uv spectrophotometry and reactions were found to be irreversible. Points of the curves in Figure 1 were achieved by time plots of the logarithm of differential absorbance measurements at any time and time zero (A_t-A_o) and consisted of two linear segments according to the biexponential Equation 1.

$$(A_t\text{-}A_o) = M \exp(b_1 t) + N \exp(b_2 t) \qquad (1)$$

where M and N are preexponential constants and b_1 and b_2 are exponential factors related to the observed rate constants of the psuedo first-order reactions.

Dissociation Constants of the Hexahydropyrimidines **I**.

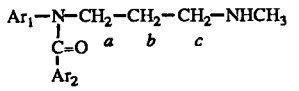
According to our proposal [4] the *p*H or H_o value at the inflection points of the curves in Figure 1 can be assumed as the pK_a value of the intermediate at the hydroxy group level [pK'_a = H_o + log (I^{3+}/I^{2+})]. This assumption is proved by the application of the Hammett modified Equation 2 [5].

$$\log(k/k_o) = a R + b F \qquad (2)$$

In fact, the plot of log k *vs.* *F* gave a straight line (Figure 2, b = 0.43, r = 0.989, s = 0.21). The term (a *R*) of Equation 2 was suppressed provided that there is not mesomeric interaction between the substituent of the

Table II

N-Aroyl-*N*-aryl-*N'*-methyltrimethylenediamines **2a-i**

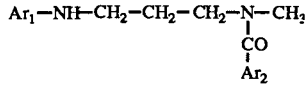


Compound No.	^{1}H NMR δ (ppm)	Multiplicity	Assignment	Picrates MP (°C)	Analyses Calcd./Found %C	%H	%N
2a	7.4-6.9	m	aromatics	114	55.53	4.63	14.08
	4.04	t	CH_2 *a*		55.50	4.70	14.03
	2.65	t	CH_2 *c*				
	2.40	s	N-CH_3				
	1.85	Q	CH_2 *b*				
	1.30	s [a]	NH				
2b	8.0	d	O_2N-C_6H_4 (2 *ortho* H)	172	50.92	4.06	15.50
					50.87	4.12	15.46
	7.7-7.0	m	aromatics				
	4.1	t	CH_2 *a*				
	2.7-1.5	m	CH_2 *c* + CH_2 *b* + N-CH_3				
	0.9	s [a]	NH				
2c	7.65-6.8	m	aromatics	181	54.65	4.74	13.28
					54.60	4.80	13.24
	3.9	t	CH_2 *a*				
	3.55	s	O-CH_3				
	2.5	t	CH_2 *c*				
	2.25	s	N-CH_3				
	1.7	Q	CH_2 *b*				
	1.3	s [a]	NH				
2d	7.3-6.75	m	aromatics	175	51.92	4.14	13.18
	3.9	t	CH_2 *a*		51.96	4.18	13.15
	2.5	t	CH_2 *c*				
	2.3	s	N-CH_3				
	1.75	Q	CH_2 *b*				
	1.2	s [a]	NH				
2e	7.6-6.65	m	aromatics (2 *ortho* H)	185	56.36	4.89	13.70
					56.32	4.95	13.67
	3.90	t	CH_2 *a*				
	2.54	t	CH_2 *c*				
	2.30	s	N-CH_3				
	2.10	s	Ar-CH_3				
	1.65	Q	CH_2 *b*				
	1.15	s [a]	NH				
2f	7.50-6.65	m	aromatics	188	59.23	4.57	12.80
	4.15	t	CH_2 *a*		59.28	4.63	12.75
	2.60	t	CH_2 *c*				
	2.40	s	CH_3				
	1.60	Q	CH_2 *b*				
	1.50	s [a]	NH				
2g [b]							
2h	7.25-6.90	m	aromatics	148	54.65	4.74	13.28
	4.0	t	CH_2 *a*		54.70	4.77	13.24
	3.7	s	O-CH_3				
	2.65	t	CH_2 *c*				
	2.40	s	NCH_3				
	2.10	Q	CH_2 *b*				
	1.55	s [a]	NH				
2i	7.10-6.90	m	aromatics	170	51.98	4.14	13.18
	3.78	t	CH_2 *a*		51.95	4.18	13.19
	2.35	t	CH_2 *c*				
	2.15	s	NCH_3				
	1.65	m [c]	CH_2 *b* + NH				

[a] Exchangeable. [b] Compound **2g** could not be satisfactorily obtained as a pure sample due to its rapid rearrangement to **3g**. [c] Upon deuteration the multiplet converts to a quintuplet.

Table III

N-Aroyl-*N*'aryl-*N*-methyltrimethylenediamines **3b-i**



Compound No.	MP (°C)	Recrystallization Solvent	Analyses Calcd./Found %C	%H	%N	IR ν (cm^{-1})		^{1}H NMR δ(ppm)	Multiplicity	Assignment
3b	104	Ethanol/ water	65.18 65.24	6.07 6.12	13.42 13.38	3340 (s) 1625 (s) 1600 (m) 1300 (m) 800 (m) 710 (m)	NH C=O C=C C-N *p*-C_6H_4 C_6H_5	8.10 7.40 6.65 5.90 3.80-3.15 1.93	d s [a] bs [b] [a] Q	O_2N-C_6H_4 (2 *ortho* H) C_6H_5 -C_6H_4-NH (2 *ortho* H) -NH -CH_2-N -C-CH_2-C
3c	98	Cyclohexane	72.48 72.42	7.38 7.45	9.40 9.36	3350 (m) 1630 (s) 1610 (m) 1280 (m) 1240 (s) 825 (m) 705 (m)	NH C=O C=C C-N C-O *p*-C_6H_4 C_6H_5	7.30 6.75-6.30 3.70-2.75 3.65 2.90 1.85	s s [a] [c] s s Q	C_6H_5 C_6H_4 CH_2-N + NH O-CH_3 N-CH_3 C-CH_2-C
3d	78	Cyclohexane	67.43 67.36	6.28 6.34	9.25 9.27	3350 (m) 1620 (s) 1600 (s) 1315 (m) 820 (m) 700 (m)	N-H C=O C=C C-N *p*-C_6H_4 C_6H_5	7.30 7.00 6.50 3.70-2.80 2.90 1.80	s d [a] [a] [c] s Q	C_6H_5 Cl-C_6H_4 (2 *ortho* H) C_6H_4-NH (2 *ortho* H) CH_2-N + NH N-CH_3 C-CH_2-C
3e	72	Cyclohexane	76.59 76.54	7.80 7.86	9.93 9.90	3350 (m) 1620 (s) 1600 (m) 1315 (m) 1300 (m) 805 (m) 700 (m)	NH C=O C=C C-N C-N *p*-C_6H_4 C_6H_5	7.30 6.90 6.50 3.70-2.80 2.95 2.14 1.85	s d [a] [a] [c] s s Q	C_6H_5 CH_3-C_6H_4 (2 *ortho* H) C_6H_4-NH (2 *ortho* H) CH_2-N + NH N-CH_3 Ar-CH_3 C-CH_2-C
3f	99	Cyclohexane	79.24 79.20	6.92 6.94	8.80 8.89	3340 (m) 1640 (s) 1610 (s) 1290 (m) 705 (m)	NH C=O C=C C-N C_6H_5	7.70-6.60 3.70-3.00 2.90 1.80	m [a] [c] s Q	aromatics CH_2N + NH N-CH_3 C-CH_2-C
3g	99	Cyclohexane	65.18 65.23	6.07 6.14	13.42 13.40	3320 (m) 1620 (s) 1590 (s) 1295 (s) 840 (s) 690 (s)	NH C=O C=C C-N *p*-C_6H_4 C_6H_5	8.25-7.90 7.60-6.95 6.75-6.40 4.0 3.75-2.80 2.90 1.85	m m m bs [b] m [a] s Q	C_6H_4-NO_2 (2 *ortho* H) aromatics C_6H_5-NH (2 *ortho* and *para* H) NH CH_2-N N-CH_3 C-CH_2-C
3h	54	Methanol/ water	72.48 72.43	7.38 7.46	9.40 9.35	3300 (m) 1615 (s) 1600 (s) 1290 (m) 820 (s) 680 (s)	NH C=O C=C C-N *p*-C_6H_4 C_6H_5	7.40-6.50 3.80 3.65-2.90 2.95 1.80	m s [a] [c] s Q	aromatics O-CH_3 CH_2-N + NH N-CH_3 C-CH_2-C

Table III (Continued)

Compound No.	MP (°C)	Recrystalization Solvent	Analyses Calcd./Found %C	%H	%N	IR ν (cm^{-1})		^{1}H NMR (ppm)	Multiplicity	Assignment
3i	64	Cyclohexane	67.43	6.28	9.26	3350 (m)	NH	7.40-7.00	m	aromatics
			67.40	6.30	9.25	1620 (s)	C=O	6.80-6.50	m	C_6H_4-NH
						1600 (s)	C=C			(2 *ortho* and *para* H)
						1310 (m)	C-N	4.15	s [b]	NH
						840 (s)	*p*-C_6H_4	3.75-2.90	[a]	CH_2-N
						690 (s)	C_6H_5	3.0	s	N-CH_3
								1.9	Q	C-CH_2-C

[a] Broad signal having poor resolution, characteristic of these compounds. [b] Exchangeable. [c] Integration diminishes upon deuteration.

phenyl group at N-1 and the -OH group of **I**. Thereby, inflection points of the curves in Figure 1 indicate that all the hydroxypyrimidines derived from **2a-f** have pK_a values close to *p*H zero except for the nitro hexahydropyrimidine (pK_a ~ -1.2). Similar pK_a values (*ca.* 0) were also found for compounds derived from **2g-i** (Figure 1). The later observations state a considerable difference with the behaviour of imidazolidine derivatives [4].

Thermodinamics of the Reactions.

Determination of the activation parameters was performed at the *p*H value corresponding to the top of each curve in Figure 1 at which concentration of protonated intermediates I^{2+} and I^{3+} are close, according to the

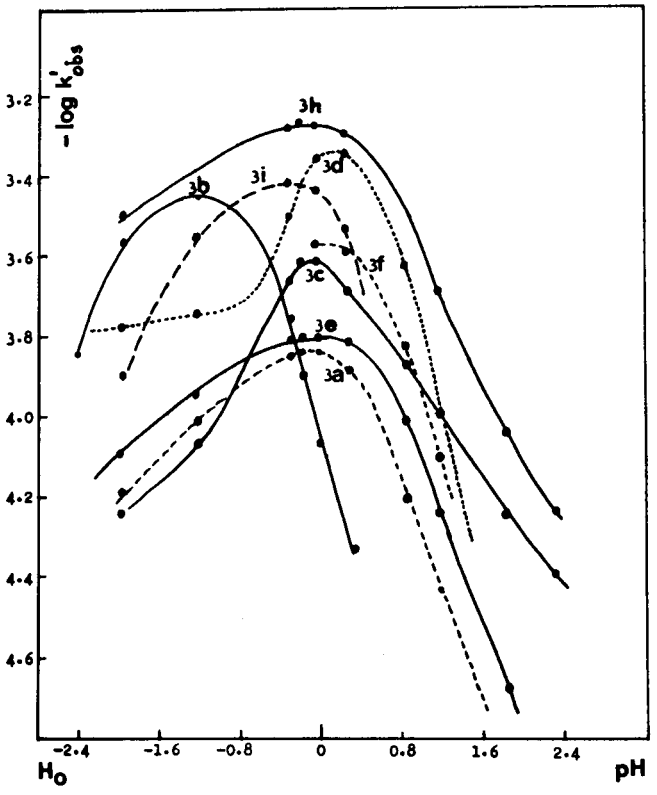


Figure 1. Rate constants of the transfer **3**→**2** in acid media. At the top of the curves the concentration of di and tri-protonated hexahydropyrimidine intermediate is close so that *p*H/H_o value can be assumed as the pK_a value of the heterocycle at the -OH group level [4].

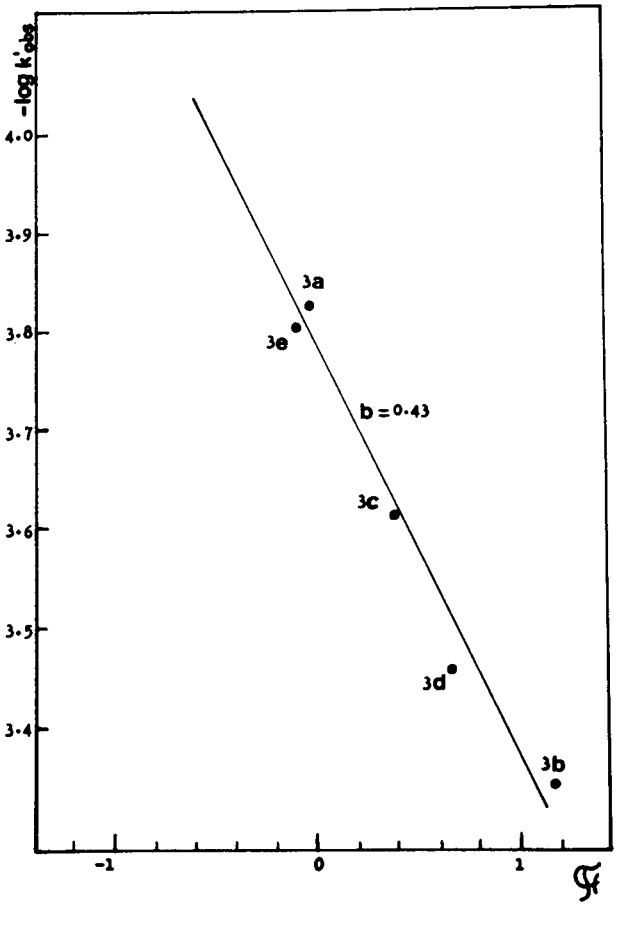
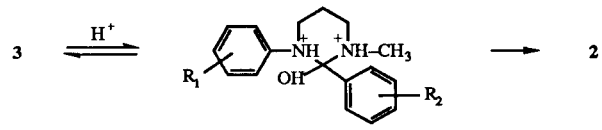


Figure 2. The Swain-Lupton analysis [10] shows the correlation between rate constants of the transfer **3**→**2** and the "field" substituent constant *F*. In this system resonance effects (*R*) must be discounted (b = 0.43, r = 0.989, s = 0.21). *F* parameters were taken from Swain *et al.* [11].

Table IV

Observed Rate Constants and Thermodynamic Parameters for the Acyl Transfer 3→2 in Acid Media at 25°



Reaction	t°C	k'_{obs} (min^{-1}) n = 2	k'_{obs} (min^{-1}) n = 3	E_{act} (Kcal/mole) n = 2	E_{act} (Kcal/mole) n = 3	$\Delta H^{\ddagger}$ (Kcal/mole) n = 2	$\Delta H^{\ddagger}$ (Kcal/mole) n = 3	$\Delta S^{\ddagger}$ (u.e.) n = 2	$\Delta S^{\ddagger}$ (u.e.) n = 3
3b→2b	25	9.12×10^{-5}	3.63×10^{-5}						
	40	1.70×10^{-4}	8.92×10^{-5}	7.10	10.92	6.53	10.36	-55.07	-44.07
	60	3.33×10^{-4}	2.61×10^{-4}						
3c→2c	25	2.62×10^{-4}	5.13×10^{-6}						
	40	4.57×10^{-4}	2.33×10^{-5}	6.21	18.20	5.64	17.74	-55.97	-23.52
	60	8.33×10^{-4}	1.50×10^{-4}						
3d→2d	25	1.33×10^{-4}	4.84×10^{-5}						
	40	2.78×10^{-4}	9.33×10^{-5}	8.22	9.06	7.65	8.50	-50.56	-49.73
	60	6.14×10^{-4}	2.63×10^{-4}						
3e→2e	25	8.32×10^{-5}	4.26×10^{-6}						
	40	1.90×10^{-4}	1.92×10^{-5}	9.64	17.73	9.08	17.17	-46.72	-25.47
	60	5.00×10^{-4}	1.19×10^{-4}						
3f→2f	25	1.58×10^{-4}	4.90×10^{-5}						
	40	2.22×10^{-4}	7.92×10^{-5}	4.31	5.87	3.75	5.30	-75.86	-60.44
	60	1.47×10^{-3}	1.44×10^{-4}						
3g→2g	25	8.32×10^{-5}	-- [a]						
		-- [a]	-- [a]	--	--	--	--	--	--
		-- [a]	-- [a]	--	--	--	--	--	--
3h→2h	25	2.01×10^{-4}	6.76×10^{-5}						
	40	2.73×10^{-4}	1.25×10^{-4}	3.46	8.45	2.90	7.88	-65.70	-51.14
	60	3.83×10^{-4}	2.75×10^{-4}						
3i→2i	25	2.34×10^{-4}	1.29×10^{-4}						
	40	9.28×10^{-4}	2.08×10^{-4}	7.54	5.90	6.97	5.33	-51.73	-58.41
	60	9.61×10^{-4}	3.80×10^{-4}						

[a] Rate constants could not be determined because hydrolysis of this particular activated benzamide is more rapid than the transfer reaction.

mechanism proposed in the Scheme II of our previous paper [4].

The higher E_{act} and $\Delta H^{\ddagger}$ values observed for six-membered compounds (n = 3) compared with those of n = 2 (Table IV) evidence a difficult opening of the hexahydropyrimidines under these experimental conditions, which is in accord with the observed lower rates for these compounds. This fact supports the decomposition of I as the rate determining step of the reaction. Concordantly, the lower $\Delta S^{\ddagger}$ values for n = 3 indicate an increased stability for the six-membered heterocycles.

EXPERIMENTAL

All melting points are uncorrected and were taken on a Büchi capillary melting point apparatus. The ir spectra were recorded on a Beckman 180A spectrophotometer. Samples were run as potassium bromide pellets for solids and films for oils. Intensity of the bands is quoted as w: weak, m: medium and s: strong. The nmr spectra were obtained on a Varian FT 80A spectrophotometer using deuteriochloroform as solvent. Chemical shifts are reported in parts per million (δ) downfield from an internal TMS reference. Signals are quoted as: s (singlet), d (doublet), t (triplet), q (quartet), Q (quintuplet), m (multiplet) and bs (broad signal). The presence of exchangeable protons was confirmed by use of deuterium oxide. The uv spectra were recorded on a Jasco 7850 spectrophotometer. Chromatograhic experiments were performed on silica gel tlc and hptlc plates.

N-Aroyl-*N'*-aryltrimethylenediamines.

The title compounds used as precursors of 1,2-diaryl-1,4,5,6-tetrahydropyrimidines, were prepared from the appropriated *N*-(3-bromopropyl)benzamide [6] and arylamines by the method of Perillo *et al.* [7]. The physical data and elementary analyses of new compounds [8] follows:

N-(*p*-Nitrobenzoyl)-*N'*-phenyltrimethylenediamine.

This compound had mp 89° (cyclohexane); ^{1}H nmr: δ 8.20 (d, 2H, $C_6H_4NO_2$, *ortho* H), 7.80 (d, 2H, $C_6H_4NO_2$, *meta* H), 7.35-7.10 (m, 2H, C_6H_5, *meta* H), 7.05 (bs, 1H, exchangeable NHCO), 6.90-6.55 (m, 3H, C_6H_5, *ortho* and *para* H), 3.90 (bs, 1H, exchangeable, N*H*Ph), 3.60 (q, 2H, C*H*$_2$-NHCO), 3.30 (t, 2H, C*H*$_2$NH-Ph), 1.95 (Q, 2H, C-CH$_2$-C).

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.21; H, 5.68; N, 14.05. Found: C, 64.17; H, 5.72; N, 14.08.

N-(*p*-Chlorobenzoyl)-*N'*-phenyltrimethylenediamine.

This compound had mp 94° (cyclohexane); ^{1}H nmr: δ 7.60 (d, 2H, C_6H_4-Cl, *meta* H), 7.40-7.05 (m, 4H, aromatics and NHCO),

6.80-6.50 (m, 3H, C_6H_5, *ortho* and *para* H), 3.95 (bs, 1H, exchangeable, N*H*-Ph), 3.55 (q, 2H, CH_2-NHCO), 3.20 (t, 2H, CH_2-NHPh); 1.90 (Q, 2H, C-CH_2-C).

Anal. Calcd. for $C_{16}H_{17}ClN_2O$: C, 66.55; H, 5.89; N, 9.70. Found: C, 66.62; H, 5.95; N, 9.74.

1,2-Diaryl-1,4,5,6-tetrahydropyrimidines.

The title compounds used as precursors of tetrahydropyrimidinium salts were prepared by ring closure of *N*-aroyl-*N'*-aryltrimethylenediamines with PPE following the general procedure reported in reference [7]. The physical data and elementary analyses of new compounds follow:

2-(*p*-Nitrophenyl)-1-phenyl-1,4,5,6-tetrahydropyrimidine.

This compound had mp 101° (cyclohexane); ^{1}H nmr: δ 8.00 (dt, 2H, NO_2-C_6H_4, *ortho* H), 7.52 (dt, 2H, $NO_2C_6H_4$, *meta* H), 7.25-6.75 (m, 5H, C_6H_5), 3.75 (q, 4H, CH_2N) and 2.05 (Q, 2H, C-CH_2-C).

Anal. Calcd. for $C_{16}H_{15}N_3O_2$: C, 68.33; H, 5.34; N, 14.94. Found: C, 68.41; H, 5.40; N, 14.88.

2-(*p*-Methoxyphenyl)-1-phenyl-1,4,5,6-tetrahydropyrimidine.

This compound had mp 84° (cyclohexane); ^{1}H nmr: δ 7.30 (d, 2H, CH_3O-C_6H_4-, *meta* H), 7.20-6.75 (m, 5H, C_6H_5), 6.65 (d, 2H, CH_3O-C_6H_4, *ortho* H), 3.75 (q, 4H, CH_2N), 3.70 (s, 3H, CH_3O) and 2.00 (Q, 2H, C-CH_2-C).

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.69; H, 6.76; N, 10.52. Found: C, 76.76; H, 6.84; N, 10.43.

2-(*p*-chlorophenyl-1-phenyl-1,4,5,6-tetrahydropyrimidine.

This compound had mp 98° (cyclohexane); ^{1}H nmr: δ 7.25 (d, 2H, ClC_6H_4, *ortho* or *meta* H), 7.20-6.72 (m, 7H, aromatics), 3.75 (q, 4H, CH_2N) and 2.00 (Q, 2H, C-CH_2-C).

Anal. Calcd. for $C_{16}H_{15}N_2Cl$: C, 70.98; H, 5.54; N, 10.35. Found: C, 71.08; H, 5.65; N, 10.30.

1,2-Diaryl-3-methyl-1,4,5,6-tetrahydropyrimidinium Iodides **1a-i**.

General Procedure.

A mixture of 0.01 mole of 1,4,5,6-tetrahydropyrimidine derivative, 0.15 mole of methyl iodide and 50 ml of methylene chloride was heated under reflux. The reaction was monitored by tlc (chloroform-methanol 9:1) following the disappearance of amidine and formation of compounds **1**. The solvent and excess of methyl iodide were removed *in vacuo*. The residue was crystallized from isopropyl alcohol affording compounds **1a-i**. Yields, melting points, recrystallization solvents, elementary analyses and spectroscopic data of compounds **1b-i** are given in Table I. Compound **1a** was described by Fernández *et al.* [2].

N-Aroyl-*N*-aryl-*N'*-methyltrimethylenediamines **2a-i**.

After dissolving compounds **1a-i** in water with the aid of heating, the resulting solution was rapidly cooled and made alkaline with 30% sodium hydroxide. The mixture of the reaction was maintained at 10°. When disappearance of **1** was observed by tlc (*ca.* 10 minutes) only one product was detected (Rf *ca.* 0.1 using chloroform-methanol 9:1 as developing solvent on hptlc silica gel plates). A methylene chloride extraction was performed at this moment. The organic layer was washed, dried and concentrated *in vacuo* keeping the reaction flask in a water bath at 18-20°, affording compounds **2a-i** [9]. In the case of compound **2b**, due to its rapid transformation in **3b**, under the experimental conditions a mixture of both products is obtained. Compound **2b** was purified dissolving the crude product in dilute hydrochloric acid and filtering to eliminate **3b**. The acid solution was brought to neutral *p*H with solid sodium carbonate and extracted with methylene chloride. The organic layer treated as above afforded pure **2b**. Attempts to obtain compounds **2** from the salts **1** and sodium carbonate or using anionic exchange resins lead to **2** and other product (Rf *ca.* 0.25 in chloroform-methanol 9:1) presumably the carbinolamine **I**.

Compounds **2a-i** are stable under acid conditions. Picrates were obtained dissolving the bases in dilute hydrochloric acid and precipitating with aqueous solution of picric acid. The resulting picrates were crystallized from ethanol. The ^{1}H nmr of the bases, melting points and elementary analyses of the picrates are given in Table II.

N-Aroyl-*N'*-aryl-*N*-methyltrimethylenediamines **3a-i**.

Compounds **2** in alkaline media spontaneously rearrange affording **3a-i** almost quantitatively after 48 hours. Compounds **3a-i** are stable in neutral or alkaline media. Under acid conditions rearrange affording **2a-i**. Melting points, recrystallization solvents, elemental analyses and spectroscopic data of compounds **3b-i** are given in Table III. Compound **3a** was described by Fernández *et al* [2].

Detection of Intermediates.

The detection of an intermediate, presumably the carbinolamine **I**, in the rearrangement **2**→**3** was performed as follows. A pure sample of **2a** was suspended in 5% sodium hydroxide. After one hour it was extracted with chloroform and the organic layer chromatographed on silica gel F_{254} hptlc plates using chloroform-methanol 9:1 as developing solvent.

Together with compounds **2a** (Rf = 0.12) and **3a** (Rf = 0.85) a third spot (Rf = 0.25) was detected under the uv light. On the other hand, a compound having the same chromatographic characteristics as the latter was detected ten minutes after that **1a** was treated with 10% sodium hydroxide at 10° and before the appearance of compound **2**. So, it can be inferred that **I** is a common intermediate in the reactions **1**→**2** and **2**→**3** (Scheme I).

Kinetic Measurements and Determination of Activation Parameters.

The same procedures employed in [4] were applied here to determine rate constants of migration and activation parameters in Table IV.

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[6] *N*-(3-Bromopropyl)-*p*-chlorobenzamide has not previously been reported. We synthesized it from *p*-chlorobenzoyl chloride and 3-bromopropylamine hydrobromide in 5% sodium hydroxide mp 92°; ^{1}H nmr: δ 7.75 (d, 2H, CO-C_6H_4, *ortho* H), 7.40 (d, 2H, CO-C_6H_4, *meta* H), 6.80 (bs, 1H, exchangeable, NH), 3.75-3.40 (m, 4H, CH_2Br and CH_2N) and 2.25 (q, 2H, C-CH_2C).

Anal. Calcd. for $C_{10}H_{11}BrClNO$: C, 43.40; H, 3.98; N, 5.06. Found: C, 43.45; H, 4.01; N, 5.09.

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