A Facile Synthesis of 2-Aryl-1,3-dimethyl-1,4,5,6-tetrahydropyrimidinium Salts

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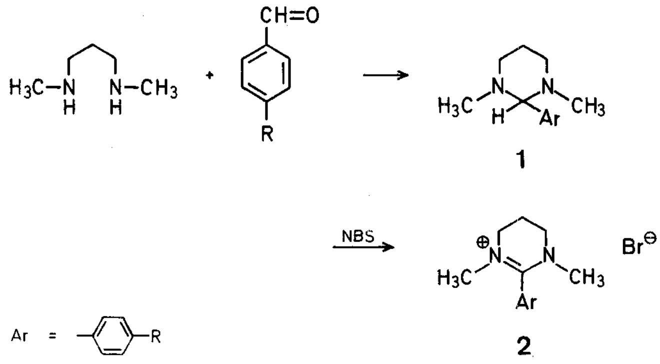
Few 1,3-dialkyl-1,4,5,6-tetrahydropyrimidinium salts have been reported, due at least in part to a lack of a simple, general method of synthesis. Heretofore, the most accessible routes have been the reaction of *N*,*N'*-dialkyl-1,3-propanediamines with amidinium salts[1] or the 3-alkylation of 1-alkyl-1,4,5,6-tetrahydropyrimidines[2]. The latter can be prepared by the reaction of *N*-alkyl-1,3-propanediamines with amidinium salts[2] or by the intramolecular dehydration of *N*-alkyl (or aryl), *N'*-acyl-1,3-propanediamines[3].

We have recently found a very convenient method for synthesizing the title compounds, namely the oxidation of 1,3-dimethylhexahydropyrimidines (**1**) with *N*-bromosuccinimide[4]. Compounds **1** are easily prepared by the condensation of *N*,*N'*-dimethyl-1,3-propanediamine with aldehydes, the latter being much more readily available than amidines.



2-Aryl-1,3-dimethylhexahydropyrimidines (1a–f):

A 500-ml flask equipped with a Dean-Stark tube and condenser is charged with aldehyde (0.25 mol), *N*,*N'*-dimethyl-1,3-propanediamine[5] (0.263 mol), *p*-toluenesulfonic acid (0.1 g), and benzene (200 ml). The mixture is heated until no additional water is collected (~2 h). After being cooled to room temperature, the reaction mixture is washed successively with 100-ml portions of 5% sodium hydroxide solution and water. The organic layer is dried over

Table 1. Synthesis of 2-Aryl-1,3-dimethylhexahydropyrimidines (**1**)

Product	R	Yield (%)	b.p./ (0.4 torr)	Elemental Analyses				
1a	H	83	67–69°	$C_{12}H_{18}N_2$	calc.	C 75.75	H 9.53	N 14.72
				(190.28)	found	75.81	9.47	14.58
1b	CH_3	89	89–90°	$C_{13}H_{20}N_2$	calc.	C 76.42	H 9.87	N 13.71
				(204.31)	found	76.46	9.79	13.61
1c	OCH_3	90	112°	$C_{13}H_{20}N_2O$	calc.	C 70.87	H 9.15	N 12.71
				(220.31)	found	71.01	9.18	12.80
1d	$N(CH_3)_2$	86	129–131°	$C_{14}H_{23}N_3$	calc.	C 72.06	H 9.93	N 18.01
			(m.p. 56°)	(233.35)	found	71.96	9.78	18.14
1e	Cl	83	102–103°	$C_{12}H_{17}ClN_2$	calc.	C 64.13	H 7.63	N 12.46
				(224.73)	found	64.21	7.65	12.27
1f	NO_2	78	106–108°	$C_{12}H_{17}N_3O_2$	calc.	C 61.26	H 7.28	N 17.86
			(m.p. 67°)	(235.29)	found	61.33	7.20	17.62

Table 2. Synthesis of 2-Aryl-1,3-dimethyl-1,4,5,6-tetrahydropyrimidinium Bromides (**2**)

Product	R	Yield (%)	m.p.	Elemental Analyses				
2a	H	76	106–107°	$C_{12}H_{17}ClN_2O_4$[a]	calc.	C 49.91	H 5.94	N 9.70
				(288.73)	found	49.86	5.89	9.78
2b	CH_3	80	119–121°	$C_{13}H_{19}BrN_2$	calc.	C 55.13	H 6.76	N 9.89
				(283.20)	found	55.19	6.81	9.80
2c	OCH_3	86	192–194°	$C_{13}H_{19}BrN_2O$	calc.	C 52.19	H 6.40	N 9.36
				(299.20)	found	52.08	6.33	9.42
2d	$N(CH_3)_2$	81	97–98°	$C_{14}H_{22}BrN_3$	calc.	C 53.85	H 7.10	N 13.46
				(312.25)	found	53.95	7.16	13.38
2e	Cl	77	129–131°	$C_{12}H_{16}BrClN_2$	calc.	C 47.47	H 5.31	N 9.26
				(303.62)	found	47.34	5.33	9.20
2f	NO_2	76	200–203°	$C_{12}H_{16}BrN_3O_2$	calc.	C 45.87	H 5.13	N 13.37
					found	45.81	4.98	13.08

[a] Perchlorate salt.

Table 3. Spectral Data on Compounds **2a–f**

Product	^{1}H-N.M.R. (D_2O), δ ppm			I.R. (KBr), cm^{-1}
	$N—CH_3$	4,6-H[a]	5-H[b]	ν(N—C—N)
2a	2.97	3.79	2.36	1660
2b	2.96	3.74	2.33	1665
2c	3.00	3.74	2.33	1665
2d	3.00	3.70	2.28	1670
2e	3.02	3.82	2.38	1660
2f	3.07	3.96	2.55	1665

[a] triplet.
[b] quintet.

sodium sulfate, the benzene is removed on a rotary evaporator, and the resulting residue is distilled under reducing pressure (Table 1).

2-Aryl-1,3-dimethyl-1,4,5,6-tetrahydropyrimidinium Bromides (2a–f):

N-Bromosuccinimide (10 mmol, recrystallized from glacial acetic acid) was added in small portions over a period of ~30 min to a stirred solution of compound **1** (10 mmol) dissolved in dry 1,2-dimethoxyethane (30 ml). The temperature of the mixture increased spontaneously to 35–40° during the course of the addition. A white precipitate began to form almost immediately. After the addition was complete, the mixture was stirred at room temperature for one hour. The reaction was conducted under a nitrogen atmosphere to protect it from moisture. The solid was collected on a filter, washed quickly with 1,2-dimethoxyethane followed by dry ether, and then recrystallized from anhydrous methanol (Table 2). Compounds **2a–e** are rather hygroscopic; the nitro derivative (**2f**) is not.

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[2] D. J. Brown, R. F. Evans, *J. Chem. Soc.* **1962**, 527.

[3] I. Perillo, S. Lamdan, *J. Heterocyclic Chem.* **10**, 915 (1973).

[4] S. Dunstan, H. B. Henbest [*J. Chem. Soc.* **1957**, 4905] have reported the use of *N*-bromosuccinimide to degrade tertiary amines to aldehydes and secondary amines.

[5] Obtained from Ames Laboratories, Milford, Conn.