Synthesis and Deamination of 1,4-Dihydronaphthalen-1,4-imines: A Convenient Naphthalene Synthesis

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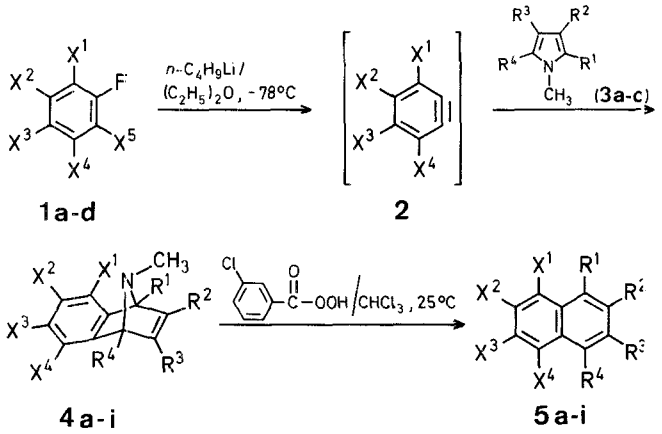
We recently reported[1] a new preparation of naphthalenes that involves the deoxygenation of 1,4-epoxy-1,4-dihydronaphthalenes with sodium borohydride in trifluoroacetic acid. The epoxydihydronaphthalenes are prepared by a Diels-Alder cycloaddition reaction between a furan and a benzyne. Since this deoxygenation does not always proceed smoothly, it was desireable to amplify this methodology by examining the deamination of the nitrogen analogs 1,4-dihydronaphthalene-1,4-imines **4** – compounds that are also useful as isoindole precursors[2,3]. We describe here the synthesis of a series of substituted naphthalen-1,4-imines **4** and their facile conversion to substituted naphthalenes **5** by treatment with *m*-chloroperbenzoic acid[4,5]. A discussion of the details of this novel deamination reaction has been previously reported[4].



The naphthalenimines **4** are conveniently prepared[6,7] via a Diels-Alder reaction between a benzyne **2**, generated from the corresponding halogenated benzene **1** and *n*-butyllithium and a pyrrole **3**. As has been noted[8], those naphthalenimines having bridgehead methyl substitution are prone to undergo hydrolytic ring-opening during workup. In these cases **(4d–i)**, the yields of **4** are relatively low (Table 1). Treatment of **4** with *m*-chloroperbenzoic acid in chloroform solution at room

Table 1. Preparation of Naphthalenimines **4**[a]

Arene[b]						Pyrrole[b]					Product	Yield [%][c]	m.p. [°C] or b.p. [°C]/torr	Molecular formula[d]
No.	X^1	X^2	X^3	X^4	X^5	No.	R^1	R^2	R^3	R^4				
1a	H	F	H	F	H	**3a**	H	H	H	H	**4c**	44	59–60°; 79–80°/0.5	$C_{11}H_9F_2N$ (193.1)
1a	H	F	H	F	H	**3b**	CH_3	H	H	CH_3	**4d**	26	102–104°/0.5	$C_{13}H_{13}F_2N$ (221.1)
1b	H	H	H	F	H	**3b**	CH_3	H	H	CH_3	**4e**	33	102–104°/0.35	$C_{13}H_{14}FN$ (203.1)
1b	H	H	H	F	H	**3c**[e]	CH_3	CH_3	CH_3	CH_3	**4f**	20	110–111°/1.0	$C_{15}H_{18}FN$ (231.1)
1c	F	F	F	F	Cl	**3b**	CH_3	H	H	CH_3	**4g**	27	86–88°/0.75	$C_{13}H_{11}F_4N$ (257.1)
1d	Cl	F	Cl	F	Cl	**3b**	CH_3	H	H	CH_3	**4h**	22	105–106°; 140°/0.25	$C_{13}H_{11}Cl_2F_2N$ (290.1)
1d	Cl	F	Cl	F	Cl	**3c**[e]	CH_3	CH_3	CH_3	CH_3	**4i**	20	143–144°/0.5	$C_{15}H_{15}Cl_2F_2N$ (318.1)
1b	H	H	H	F	H	**6**[f]					**7**[g]	12	84–85°	$C_{17}H_{20}FN$ (257.1)
											8[g]	17	59–60°	$C_{17}H_{20}FN$ (257.1)

[a] The preparation of **4a** and **4b** was described previously[7].
[b] Commercially available unless otherwise noted.
[c] Yield of isolated and purified material.
[d] All products gave satisfactory microanalyses (C ±0.09%, H ±0.09%, N ±0.06%, Cl ±0.01%) except for **4f** and **4i**, which were characterized by mass spectometry.
[e] Prepared by refluxing a benzene solution of 3,4-dimethylhexane-2,5-dione[9] and methylamine.
[f] Prepared by a Wolff-Kishner reduction of 1,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindole[10].
[g] Separated by medium pressure liquid chromatography.

Table 2. Preparation of Naphthalenes **5**

Substrate									Product[a]	Yield [%][b]	m.p. [°C] or b.p. [°C]/torr	Molecular formula[c] or Lit. m.p. or b.p.	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
No.	X^1	X^2	X^3	X^4	R^1	R^2	R^3	R^4					
4a[7]	Cl	F	Cl	F	H	H	H	H	**5a**	75	105–106°	103–104°[7]	
4b[7]	F	F	F	F	H	H	H	H	**5b**	96	107–109°	108–110°[7]	
4c	H	F	H	F	H	H	H	H	**5c**	84	32–34°/0.25	39–40°/0.02[11]	
4d	H	F	H	F	CH_3	H	H	CH_3	**5d**	79	87–88°/0.25	87–88°/0.25[1]	
4e	H	H	H	F	CH_3	H	H	CH_3	**5e**	64	70–73°/0.5	70–73°/0.5[1]	
4f	H	H	H	F	CH_3	CH_3	CH_3	CH_3	**5f**	61	107–108°	$C_{14}H_{15}F$ (202.2)	2.17 (s, 6H); 2.36 (s, 3H); 2.62 (d, 3H, J=6.6 Hz); 7.2 (m, 3H)
4g	F	F	F	F	CH_3	H	H	CH_3	**5g**	90	129–130°	124–127°[8]	
4h	Cl	F	Cl	F	CH_3	H	H	CH_3	**5h**	73	155–156°	155–156°[1]	
4i	Cl	F	Cl	F	CH_3	CH_3	CH_3	CH_3	**5i**	40	140–141°	$C_{14}H_{12}Cl_2F_2$ (289.1)	2.33 (s, 6H); 2.46 (s, 3H); 2.63 (s, 3H)
7									**9**	93	155–165°/0.4	$C_{16}H_{17}F$ (228.2)	1.06 (s, 6H); 1.61 (t, 2H, J=7.3 Hz); 2.82 (s, 2H); 2.92 (t, 2H, J=7.3 Hz); 7.0–7.9 (m, 5H)
8									**10**	92	114–118°/0.15	$C_{16}H_{17}F$ (228.2)	1.00 (s, 6H); 1.50 (t, 2H, J=7 Hz); 2.90 (t, 2H, J=7 Hz); 3.10 (d, 2H, J=5.1 Hz); 6.8–7.5 (m, 5H)

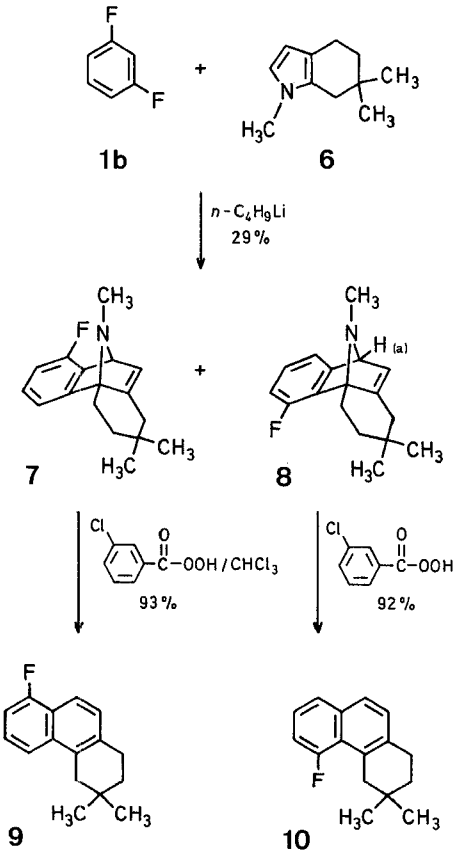
[a] Products were identified by ^{1}H-N.M.R. spectra and where possible by direct comparison with known[1,7] samples or by comparison with literature data.

[b] Yield of isolated and purified material.

[c] Naphthalenes **5f** and **5i** gave satisfactory microanalyses (C ±0.06%, H ±0.03%, Cl ±0.04%) and **9** and **10** were characterized by high resolution mass spectrometry: **9**, m/e=228.1323; **10**, m/e=228.1314 (M^+ calc. 228.1314).

temperature affords the corresponding naphthalene **5** in good to excellent yield (Table 2). Hart et al.[5] have reported the influence of different solvents on this deamination reaction but we find that chloroform usually works well. The naphthalenes **5** can be readily purified by column chromatography and then distillation or recrystallization. Using this methodology, we have prepared several new naphthalenimines **(4c–i)** and two new naphthalenes **(5f, i)**.

The methodology can be applied to the construction of related ring systems. Thus, we have also synthesized the isomeric tetrahydrophenanthrenes **9** and **10**, as shown below.



The individual imines **7** and **8** were identified by the existence of a five-bond zig-zag proton(Ha)-fluorine spin-spin coupling in **8** but not in **7**[12].

1,4-Dihydronaphthalen-1,4-imines 4; General Procedure:
To a magnetically stirred solution of arene **1** (0.05 mol) in dry ether (250 ml) at −78 °C under nitrogen is added dropwise over 0.5 h *n*-butyllithium (1.55 molar solution in hexane; 0.05 mol). The mixture is stirred for 1 h at −78 °C and then treated dropwise with a solution of pyrrole **3** (0.07 mol) in dry ether (100 ml). The mixture is stirred at −78 °C for 1 h and then allowed to warm to room temperature overnight. The reaction mixture is extracted with cold 1 normal hydrochloric acid (5 × 50 ml) and the combined acidic extracts are basified with cold 50% aqueous sodium hydroxide solution. The basic solution is extracted with ether (5 × 50 ml), the extract is dried with anhydrous sodium sulfate, and concentrated in vacuo. The crude product is column chromatographed (basic alumina activity III) and then further purified by either recrystallization or distillation to give **4** (Table 1).

Naphthalenes 5 by Deamination of 4; General Procedure:
To a magnetically stirred solution of naphthalenimine **4** (0.01 mol) in chloroform (50 ml) at 25 °C under nitrogen is added in one portion *m*-chloroperbenzoic acid (0.02 mol). The reaction mixture, which may be conveniently monitored by thin layer chromatography, is stirred at room temperature for 24 h and then concentrated in vacuo. The residue is column chromatographed (basic alumina activity III) and then further purified by either recrystallization or distillation to give **5** (Table 2).

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