One-Carbon Ring Enlargement by Rearrangement of Ammonium Halides

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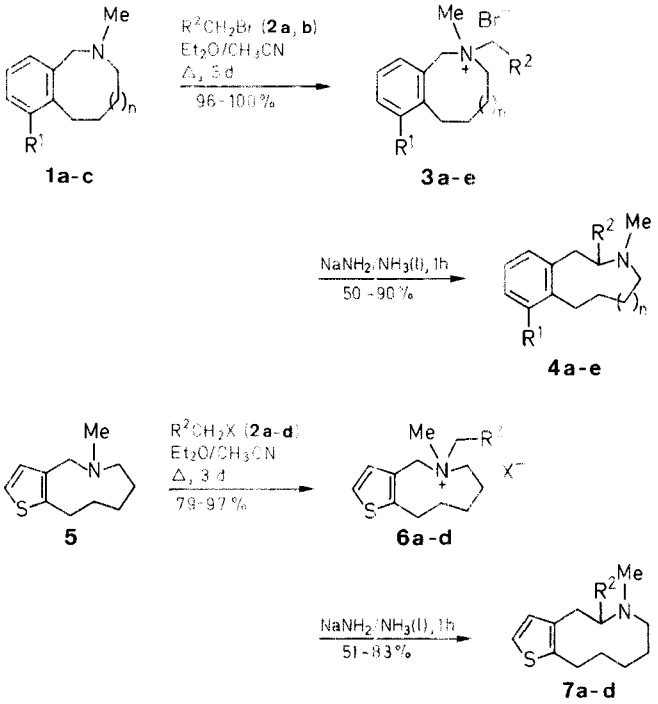
Treatment of *N*-allyl- or (benzyl or thenyl)*N*-methyl-1,2,3,4,5,6-hexahydro-2-benzazocinium, the corresponding 2-benzazoninium, or 5,6,7,8,9,10-hexahydro-4*H*-thieno[3,2-*c*]azoninium salts with sodium amide in liquid ammonia affords, as the sole product, the derivative arising from one-carbon ring enlargement by a Stevens reaction.

Rearrangement of ammonium ylides may follow three different ways: α',β-elimination, 1–2 migration (Stevens reaction), and 2–3 migration (Sommelet–Hauser reaction); the later is favored when the reaction is conducted in liquid ammonia with sodium amide.[1] This was observed starting from *N*-methyl *N*-alkyl derivatives with hexahydrobenzazoninium ylides, which afford mainly azacyclophanes,[2] and with hexahydrothienoazoninium, which lead to spirocompounds;[3] hexahydrobenzazocinium ylides allow an unexpected synthesis of enamines.[4]

In this paper, we report that all these compounds lead solely to ring enlargement of one carbon by Stevens reaction when the nitrogen atom bears a methyl group and one β,γ-unsaturated group (allyl, benzyl or thenyl).

The structures of the products have been established by ^{1}H- and ^{13}C-NMR spectroscopy; all the signals have been assigned by proton–proton and proton–carbon correlated spectra.

When the *N*-benzyl group of the ammonium salt is *ortho*-substituted, the reaction is no longer selective and leads to a mixture of products.



1	n	R^1	2, 6, 7	R^2	X
a	1	H	a	CH_2=CH	Br
b	1	CH_3	b	Ph	Br
c	2	H	c	2-thienyl	I
			d	3-thienyl	I

3, 4	n	R^1	R^2
a	1	H	CH_2=CH
b	1	CH_3	CH_2=CH
c	1	H	Ph
d	1	CH_3	Ph
e	2	H	CH_2=CH

Table 1. Hexahydro-2-benzazocinium (**3a–d**), -benzazoninium (**3e**), and -thienoazoninium (**6a–d**) Halides Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]
3a	96	198	$C_{15}H_{22}BrN$ (296.3)
3b	97	202	$C_{16}H_{24}BrN$ (310.3)
3c	97	219–220	$C_{19}H_{24}BrN$ (346.3)
3d	97	250	$C_{20}H_{26}BrN$ (360.3)
3e	100	176–177	$C_{16}H_{24}BrN$ (310.3)
6a	79	185	$C_{14}H_{22}BrNS$ (316.3)
6b	97	197	$C_{18}H_{24}BrNS$ (366.4)
6c	90	194	$C_{16}H_{22}INS_2$ (419.4)
6d	97	184	$C_{16}H_{22}INS_2$ (419.4)

[a] Satisfactory microanalyses obtained: C ±0.35, H ±0.32, Br ±0.33, I ±0.18, N ±0.35, S ±0.20; except **3a** (Br −0.61), **3b** (C −0.8), **6b** (C −0.49).

Starting compounds **1a–c** and **5** have been previously described.[5,6]

2-Allyl-2-methyl-2,3,4,5,6,7-hexahydro-1*H*-2-benzazoninium Bromide (3e); Typical Procedure:

A mixture of the 2-methyl-2,3,4,5,6,7-hexahydro-1*H*-2-benzazonine (**1c**; 1.89 g, 10 mmol) and allyl bromide (**2a**; 2.4 g, 20 mmol) in anhydrous ether (30 mL) and acetonitrile (10 mL) is refluxed for 3 d; the precipitate of ammonium salt **3e** is then filtered and dried *in vacuo*; yield: 3.1 g (100%); mp 176–177°C.

3-Methyl-2-vinyl-1,2,3,4,5,6,7,8-octahydro-3-benzazecine (4e); Typical Procedure:

In a 250 mL three-necked flask equipped with a mechanical stirrer, a cooled MeOH condenser and a thermometer, a small piece of clean Na metal is added to anhydrous liq. NH_3 (100 mL); a few crystals of iron(III) nitrate hydrate are added, whereon the blue color is discharged; the rest of the Na (total: 0.46 g, 0.02 g atom) is then rapidly added. When all the Na has been transformed, the benzazoninium bromide **3e** (3.1 g, 10 mmol) is added, and the mixture is stirred for 1 h

Table 2. Hexahydro-1*H*-3-benzazonines **4a–d**, Octahydro-3-benzazecine **4e**, and Octahydrothieno[3,2-*d*]azecines **7a–d**

Product	Yield (%)	bp (°C)/Torr	Molecular Formula[a]	^{1}H-NMR ($CDCl_3$/TMS)[b] δ	^{13}C-NMR ($CDCl_3$/TMS) δ
4a	53	105/2	$C_{15}H_{21}N$ (215.3)	1.4–1.5 (m, 1H, H-5); 1.5–1.65 (m, 2H, H-5 and H-6); 1.8–1.95 (m, 1H, H-6); 1.95–2.2 (m with s at 2.06, 4H, NMe and H-4); 2.55–2.65 (m, 3H, H-1 and H-7); 2.9–3.2 (m, 3H, H-1, H-2 and H-4); 5.1–5.3 (m, 2H, H-2'); 5.6–5.75 (m, 1H, H-1'); 7.06 (m, 4H_{arom})	25.6 (t), 27.0 (t), 28.4 (t), 37.4 (t), 41.2 (q), 45.4 (t), 68.8 (d), 115.8 (t), 125.3 (d), 126.1 (d), 129.4 (d), 130.1 (d), 136.9 (d), 138.0 (s), 145.0 (s)[c]
4b	50	105/0.25	$C_{16}H_{23}N$ (229.4)	1.4–1.5 (m, 2H, H-5 and H-6); 1.55–1.65 (m, 1H, H-5); 1.9–2.4 (m with s at 2.26, 5H, NMe, H-4 and H-6); 2.42 (s, 3H, ArMe); 2.5–2.65 (m, 3H, H-1 and H-7); 2.9–3.2 (m, 3H, H-1, H-2 and H-4); 5.1–5.3 (m, 2H, H-2'); 5.6–5.75 (m, 1H, H-1'); 7.01 (m, 4H_{arom})	20.4 (q), 23.9 (t), 24.8 (t), 25.5 (t), 37.6 (t), 41.2 (q), 44.6 (t), 69.3 (d), 113.8 (t), 125.0 (d), 128.0 (d), 128.1 (d), 135.4 (s), 136.8 (d), 138.2 (s), 143.9 (s)[b]
4c	90	145/1	$C_{19}H_{23}N$ (265.4)	1.4–1.5 (m, 1H, H-5); 1.5–1.7 (m, 2H, H-5 and H-6); 2–2.15 (m with s at 2.1, 5H, H-4, H-6 and NMe); 2.65–2.75 (m, 2H, H-1 and H-7); 2.75–2.9 (m, 1H, H-7); 3.2–3.5 (m, 1H, H-4); 3.6–3.7 (m, 2H, H-1 and H-2); 7.0–7.5 (m, 9H_{arom})	25.1 (t), 27.1 (t), 28.8 (t), 37.2 (t), 41.2 (q), 45.8 (t), 70.0 (d), 125.6 (d), 126.8 (d), 127.9 (d), 129.6 (d), 130.3 (d), 139.3 (s), 140.8 (s), 144.7 (s)[c]
4d	77	125/0.1	$C_{20}H_{25}N$ (279.4)	1.5–1.65 (m, 2H, H-5 and H-6); 1.65–1.75 (m, 1H, H-5); 1.75–1.9 (m, 1H, H-4); 2.05–2.2 (m with s at 2.12, 4H, H-6 and NMe); 2.4 (s, 3H, ArMe); 2.7–2.8 (m, 3H, H-1 and H-7); 3.4–3.5 (m, 1H, H-4); 3.6–3.7 (m, 2H, H-1 and H-2); 7–7.5 (m, 8H_{arom})	20.4 (q), 24.2 (t), 25.0 (t), 37.2 (t), 41.2 (q), 44.7 (t), 70.4 (d), 125.3 (d), 126.8 (d), 127.9 (d), 128.2 (d), 135.7 (s), 139.3 (s), 140.4 (s), 143.8 (s)[c]
4e	50	106/0.2	$C_{16}H_{23}N$ (229.4)	1.08 (m, 1H, H-6); 1.28 (m, 1H, H-5); 1.46 (m, 1H, H-6); 1.70 (m, 2H, H-6 and H-7); 2.00 (s, 3H, NMe); 2.05 (m, 3H, H-4 and H-7); 2.50 (m, 1H, H-1); 2.64 (m, 1H, H-8); 2.95 (m, 1H, H-8); 3.05 (m, 2H, H-1 and H-4); 3.18 (m, 1H, H-2); 5.15, 5.20 (m, 2H, H-2'); 5.83 (m, 1H, H-1'); 7.05–7.25 (m, 4H_{arom})	18.3 (t), 28.1 (t), 29.8 (t), 31.5 (t), 35.2 (t), 40.5 (q), 46.9 (t), 70.4 (d), 116.3 (t), 125.2 (d), 125.6 (d), 128.1 (d), 129.3 (d), 136.5 (d), 139.1 (s), 141.1 (s)[c]
7a	83	113/0.4	$C_{14}H_{21}NS$ (235.4)	1.10 (m, 1H, H-9); 1.25 (m, 1H, H-8); 1.55 (m, 1H, H-9); 1.70 (m, 2H, H-8 and H-10); 1.90 (m, 1H, H-10); 2.00 (m, 1H, H-7); 2.03 (s, 3H, NMe); 2.60 (m, 1H, H-4); 2.80 (m, 2H, H-4 and H-11); 2.90 (m, 1H, H-7); 3.00 (m, 1H, H-11); 3.10 (m, 1H, H-5); 5.15 (m, 2H, H-2'); 5.80 (m, 1H, H-1'); 6.77 (m, 1H, H-3); 7.07 (m, 1H, H-2)	17.7 (t), 27.0 (t), 27.8 (t), 31.6 (t), 33.0 (t), 40.2 (q), 46.6 (t), 68.2 (d), 116.4 (t), 121.6 (d), 128.1 (d), 135.8 (s), 136.6 (d), 140.2 (s)[b]
7b	56	132/0.4	$C_{18}H_{23}NS$ (285.5)	1.22 (m, 1H, H-9); 1.30 (m, 1H, H-8); 1.64 (m, 1H, H-9); 1.70 (m, 2H, H-8 and H-10); 1.90 (m, 1H, H-10); 1.97 (s, 3H, NMe); 2.17 (m, 1H, H-7); 2.70 (m, 1H, H-4); 2.90 (m, 1H, H-11); 3.15 (m, 2H, H-7 and H-11); 3.30 (m, 1H, H-4); 3.75 (m, 2H, H-5); 6.83 (m, 1H, H-3); 7.15 (m, 1H, H-2); 7.22–7.39 (m, 4H_{arom})	17.9 (t), 27.3 (t), 27.8 (t), 31.1 (t), 33.2 (t), 40.2 (q), 47.0 (t), 69.7 (d), 121.7 (d), 127.0 (d), 127.8 (d), 128.0 (d), 128.2 (d), 136.5 (s), 139.0 (s), 140.5 (s)[b]
7c	51	147/0.1	$C_{16}H_{21}NS_2$ (291.5)	1.17 (m, 1H, H-9); 1.30 (m, 1H, H-8); 1.58 (m, 1H, H-9); 1.60 (m, 1H, H-10); 1.70 (m, 1H, H-8); 1.75 (m, 1H, H-10); 1.95 (m, 1H, H-7); 2.03 (s, 3H, NMe); 2.85 (m, 1H, H-4); 2.90 (m, 1H, H-11); 3.03 (m, 1H, H-7); 3.11 (m, 1H, H-11); 3.20 (m, 1H, H-4); 4.10 (m, 1H, H-5); 6.83 (m, 1H, H-3); 6.90 (m, 1H, H-3'); 7.01 (m, 1H, H-4'); 7.13 (m, 1H, H-2); 7.21 (m, 1H, H-5')	17.9 (t), 27.2 (t), 27.7 (t), 33.0 (t), 33.1 (t), 40.2 (q), 47.0 (t), 64.7 (d), 121.9 (d), 123.9 (d), 124.9 (d), 126.2 (d), 127.9 (d), 136.0 (s), 140.8 (s), 142.2 (s)[b]
7d	53	182/0.4	$C_{16}H_{21}NS_2$ (291.5)	1.19 (m, 1H, H-9); 1.32 (m, 1H, H-8); 1.61 (m, 1H, H-9); 1.67 (m, 1H, H-10); 1.76 (m, 2H, H-8 and H-10); 1.98 (m, 1H, H-7); 2.03 (s, 3H, NMe); 2.73 (m, 1H, H-4); 2.88 (m, 1H, H-11); 3.07 (m, 1H, H-7); 3.12 (m, 1H, H-11); 3.21 (m, 1H, H-4); 3.90 (m, 1H, H-5); 6.82 (m, 1H, H-3); 7.03 (m, 1H, H-4'); 7.06 (m, 1H, H-2'); 7.13 (m, 1H, H-2); 7.28 (m, 1H, H-5')	17.9 (t), 27.2 (t), 27.6 (t), 31.7 (t), 33.1 (t), 40.4 (q), 47.1 (t), 64.7 (d), 121.2 (d), 121.7 (d), 124.5 (d), 127.5 (d), 128.0 (d), 136.3 (s), 140.5 (s), 140.6 (s)[b]

[a] The microanalyses were in satisfactory agreement with the calculated values: C ± 0.36, H ± 0.26, N ± 0.27, S ± 0.20; except **4a** (C + 0.49, H − 0.46), **4c** (C − 0.91), **4d** (C − 0.90).

[b] Recorded on a Bruker AM 400 spectrometer.

[c] Recorded on a Bruker WP 80 spectrometer.

and neutralized with NH_4Cl (1.7 g, 20 mmol). The ammonia is evaporated; the residue is washed with water (10 mL) and extracted with ether (3 × 10 mL). The organic layer is dried (K_2CO_3) and distilled to give **4e**; yield: 1.15 g (50%) (bp 106 °C/0.2 Torr); and 1.2 g of tarry residue.

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