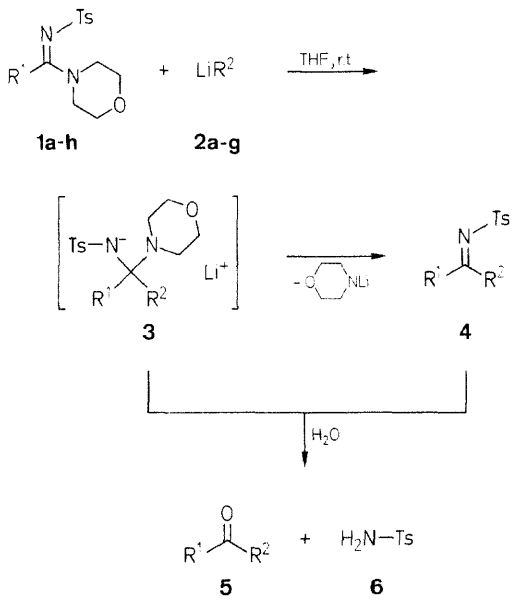

N-Arylsulfonylamidines; Part 2.[1] A New Synthesis of Ketones from *N'*-Tosylamidines and Organolithium Compounds

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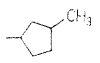
Tertiary *N'*-arylsulfonylamidines readily react with organolithium compounds under simple conditions to afford carbonyl compounds.

Tertiary *N'*-arylsulfonylamidines are readily obtained from enamines by cycloaddition with arylsulfonyl azides and rearrangement with N_2-elimination of the unstable triazoline intermediates.[2-4]

As a part of our program on the synthetic possibilities of this class of compounds, we now report a new ketone synthesis starting from amidines (**1**) and alkyl-, aryl-, or heteroaryllithium compounds (**2**).

Tosylamidines **1a–g** readily reacted with organolithium compounds **2a–g** in anhydrous tetrahydrofuran at room temperature (1–3 h). The lithium derivatives **2** were used as commercial solutions or were prepared before use from the corresponding heterocycles according to standard procedures. Compounds **2** were used in a two-fold molar excess since this was found to afford the best yields of ketones **5**. Chromatographic purification of the reaction mixture afforded ketones **5** as the main reaction products. Tosylamine (**6**) was also formed but generally not isolated. Ketones **5** were easily identified on the basis of analytical and spectroscopic properties (Table). In some cases, besides **5** and **6** a minor amount of compounds **4** was obtained. In the case of compounds **4ab** and **4ag** in which the group R bears an hydrogen atom on C-1, the more stable enamine tautomers were obtained. Compounds **4** were identified on the basis of analytical and IR data (Table). A further confirmation of their structure was obtained by hydrochloric acid-catalyzed hydrolysis which afforded **6** and the corresponding ketones **5**.

The reaction of lithium compounds **2** with substrates **1** is rationalized by assuming nucleophilic attack of the lithium derivative on the amidine C-atom producing the anionic intermediate **3** from which the *N*-tosylimine **4** (or the corresponding enamine tautomer) is formed through elimination of morpholine. The main products **5** are formed as hydrolysis products of imines **4** during work-up or directly from the hydrolysis of salts **3**.

1	R^1	**2**	R^2
a	*cyclo*-C_5H_9	**a**	C_6H_5
b		**b**	
c	*cyclo*-C_3H_8	**c**	
d		**d**	
e	2-thienyl	**e**	*n*-C_4H_9
f	$-CH(CH_3)CH_2CH_3$	**f**	CH_3
g	C_2H_5	**g**	2-thienyl
h	H		

It was expected that starting from formamidine **1h** aldehydes could be obtained as products. It was indeed observed that aldehydes **5hc** and **5hd** were formed. However, the yields were only poor.

On the whole, the reaction can be considered of synthetic interest, mainly for the preparation of heterocyclic ketones, by virtue of the good availability of the starting compounds and the simple reaction conditions.

Most amidines have been described previously (**1a**,[1] **1c**,[4] **1e**,[5] **1f**,[2] **1g**,[1] **1h**,[6]). The new amidines were obtained by a described procedure[2,3,4] from the corresponding enamines[7,8,9] and tosyl azide:

N'-Tosylamidine **1b**; yield: 30%; m.p. 82 °C.

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.90–1.50 (m, 10H); 2.40 (s, 3H); 3.90–4.40 (m, 1H); 3.50–4.80 (m, 8H); 7.10–7.30 (m, $2H_{arom}$); 7.60–7.85 (m, $2H_{arom}$).

N'-Tosylamidine **1d**; yield: 70%; m.p. 132 °C.

^{1}H-NMR ($CDCl_3$/TMS): δ = 2.4 (s, 3H); 3.4 (s, 3H); 3.4–3.7 (m, 8H); 6–6.1 (m, $2H_{pyrrole}$); 6.4–6.6 (m, $1H_{pyrrole}$); 7–7.3 (m, $2H_{tosyl}$); 7.4–7.6 (m, $2H_{tosyl}$).

The lithium compounds were commercial products (**2a**, **2e**, **2f**) or were prepared from the corresponding heterocycles according to published methods.[10,11]

Table. Products **5** (and **4**) Obtained from the Reaction of *N*-Tosylamidines **1** with Organolithium Compounds **2**

Starting Compounds	Products	Yield[a] (%)	m.p. (°C) or b.p. (°C)/Torr[b]	Molecular Formula[c] or Lit. Data	IR (nujol) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[d] δ
1a + 2a	**5aa**	78	140/15	b.p. 136–140/16[12]	1720 (C=O)	1.55–2.15 (m, 8H); 3.5–3.9 (m, 1H); 7.35–8.1 (m, 5H$_{arom}$)
1a + 2b	**4ab**	5	98–100	$C_{19}H_{22}N_2SO_2$ (342.4)	1600, 1640 (–CH=C–NH–)	1.3–2.1 (m, 8H); 2.4 (s, 3H); 3.0–3.3 (m, 1H); 5.5 (s, 1H); 6.9–7.9 (m, 7H$_{arom}$); 8.4–8.6 (m, 1H$_{pyridine}$); 13.6 (s, 1H, NH, exchangeable)
	5ab	44	210/0.3	$C_{12}H_{15}NO$ (189.2)	1710 (C=O)	1.2–2.0 (m, 8H); 2.85–3.25 (m, 1H); 3.9 (s, 2H); 7.0–7.75 (m, 3H$_{pyridine}$); 8.5–8.65 (m, 1H$_{pyridine}$)
1a + 2c	**5ac**	31	260–270/0.5	$C_{15}H_{17}NO_2$ (243.3)	1670 (C=O)	1.60–2.2 (m, 8H); 3.5–3.9 (m, 1H); 4.1 (s, 3H); 7.0–7.7 (m, 5H$_{indole}$)
1a + 2d	**5ad**	54	170–175/0.4	$C_{11}H_{15}NO$ (177.2)	1650 (C=O)	1.2–2.2 (m, 8H); 3.35–3.75 (m, 1H); 4.0 (s, 3H); 6.0–6.2 (m, 1H$_{pyrrole}$); 6.8–7.0 (m, 2H$_{pyrrole}$)
1a + 2e	**5ae**	36	40–60/0.1	b.p. 104–106/25[14]	1710 (C=O)	0.8–2.0 (m, 15H); 2.35–2.6 (m, 2H); 2.7–3.1 (m, 1H)
1a + 2f	**5af**	37	158/15	b.p. 159–160/760[15]	1710 (C=O)	1.4–2.0 (m, 8H); 2.2 (s, 3H); 2.75–3.15 (m, 1H)
1a + 2g	**4ag**	12	148	$C_{17}H_{19}NS_2O_2$ (333.4)	1600, 1640 (–CH=C–NH–)	1.45–1.85 (m, 4H); 2.2–2.65 (m, 7H); 5.95 (s, NH, exchangeable); 6.7–7.7 (m, 7H$_{arom}$)
	5ag	63	90/1	b.p. 128–129/7[16]	1660 (C=O)	1.55–2.2 (m, 8H); 3.4–3.75 (m, 1H); 7.0–7.75 (m, 3H$_{thiophene}$)
1b + 2d	**5bd**	32	180/0.5	$C_{12}H_{17}NO$ (191.3)		0.9–2.3 (m, 9H); 3.4–3.8 (m, 1H); 4.0 (s, 3H); 6.0–6.15 (m, 1H$_{arom}$); 6.7–7.0 (m, 2H$_{arom}$)
1c + 2a	**5ca**	15	130/15	b.p. 116–117/10.5[13]	1720 (C=O)	0.9–1.3 (m, 4H); 2.5–2.85 (m, 1H); 7.1–8.1 (m, 5H$_{arom}$)
1d + 2d	**5dd**	32	130/1	b.p. 305–307/755[17]	1610 (C=O)	4.0 (s, 6H); 6.0–6.15 (m, 2H$_{pyrrole}$); 6.7–6.95 (m, 4H$_{pyrrole}$)
1e + 2g	**5eg**	45	88	m.p. 90–90.5[18]	1610 (C=O)	7.0–7.3 (m, 2H$_{thiophene}$); 7.55–7.75 (m, 2H$_{thiophene}$); 7.8–8.0 (m, 2H$_{thiophene}$)
1f + 2d	**4fd**	13	85–86	$C_{17}H_{22}N_2SO_2$ (318.4)	1600 (C=N)	0.8–1.1 (m, 3H); 1.6–1.8 (m, 3H); 1.9–2.3 (m, 2H); 2.45 (s, 3H); 3.3 (s, 3H); 5.7–6.1 (m, 3H); 6.4 (m, 1H$_{pyrrole}$); 7.0–7.5 (m, 4H$_{arom}$)
	5fd	46	120/1	$C_{10}H_{15}NO$ (165.2)	1645 (C=O)	0.8–1.0 (m, 3H); 1.0–1.25 (m, 3H); 1.3–2.2 (m, 2H); 3.0–3.3 (m, 1H); 3.9 (s, 3H); 6.0–6.2 (m, 1H$_{pyrrole}$); 6.7–7.0 (m, 2H$_{pyrrole}$)
1g + 2c	**4gc**	16	110–112	$C_{19}H_{20}N_2SO_2$ (340.4)	1540, 1590 (C=N)	1.35–1.65 (m, 3H); 2.45 (s, 3H); 3.25–3.7 (m, 2H); 3.85 (s, 3H); 7.0–8.05 (m, 9H$_{arom}$)
	5gc	10	48–50	$C_{12}H_{13}NO$ (187.2)	1660 (C=O)	1.1–1.4 (m, 3H); 2.85–3.2 (m, 2H); 4.1 (s, 3H); 7.0–7.8 (m, 5H$_{indole}$)
1h + 2c	**5hc**	12	150/0.1	b.p. 90–92/0.02[19]	1665 (H–C=O)	4.1 (s, 3H); 7.1–7.9 (m, 5H$_{indole}$); 9.8 (s, 1H)
1h + 2d	**5hd**	10	80/15	b.p. 94–96/32[20]	1655 (H–C=O)	4.0 (s, 3H); 6.0–6.2 (m, 1H$_{pyrrole}$); 6.7–7.0 (m, 2H$_{pyrrole}$); 9.5 (s, 1H)

[a] Not optimized.
[b] Not corrected.
[c] Satisfactory microanalyses obtained: C ±0.28, H ±0.35, N ±0.21.
[d] Recorded on Varian 360A spectrometer.

Ketones 5 (or Aldehydes 5hc, 5hd) from *N,N*-(3-Oxa-1,5-pentanediyl)-*N'*-tosylamidines (1) and Organolithium Compounds (2); General Procedure:

The *N'*-tosylamidine **1** (15 mL) is suspended in anhydrous THF (40–50 mL) and a solution of the organolithium compound **2** (30 mL) in Et_2O or THF or hexane is added dropwise, with stirring at room temperature, over a period of ~10 min. A moderate temperature increase is observed in some cases. The mixture is stirred until complete reaction of the starting **1** is evidenced by TLC (eluent CH_2Cl_2). Then, methanol (10 mL) is added and the mixture is evaporated under reduced pressure. The residue is chromatographed on a silica gel column (petroleum ether/CH_2Cl_2 gradient) yielding a main fraction which is evaporated affording the crude product **5**. In some cases, another fraction containing **4** is obtained. Compounds **5** are purified by distillation or recrystallization.

Received: 21 April 1987

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