## An Easy Synthesis of Electron-withdrawing Substituted 2-Aza-1,3-dienes and their 1,4-Cycloaddition with Enamines

## José Barluenga\*, Miguel Tomás, Alfredo Ballesteros, and Vicente Gotor

Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

An easy procedure for the synthesis of electron-poor 2-aza-1,3-dienes from silylimines is described; the ability of these azadienes to undergo cycloaddition to electron-rich alkenes is demonstrated for the first time.

The [4 + 2] cycloadditions of aza-1,3-dienes have been much less investigated than those of the corresponding all-carbon systems.<sup>1</sup> It has been reported that electron-donating substituted 2-azadienes react with electron-poor dienophiles to form pyridine derivatives;<sup>2</sup> furthermore, we have developed an easy route to electronically neutral 2-azadienes and have demonstrated their ability to undergo normal [4 + 2]cycloaddition reactions.<sup>3</sup> However, the potential value of 2-azadienes with appended electron-withdrawing substituents remains unexplored, probably owing to the lack of general methods of synthesis of these heteradienes;<sup>†</sup> the dimerization<sup>5</sup> of the highly reactive 1-biphenylyl-3-methoxycarbonyl-2-aza-1,3-diene prepared from the Schiff's base of serine methyl ester<sup>6</sup> appears to be the sole example of a [4 + 2] cycloaddition of a simple system.

Taking advantage of the fact that the imino nitrogen-silicon bond is capable of adding to the carbon-carbon triple bond of activated acetylenes,<sup>7</sup> we have developed an easy route to the 3,4-bismethoxycarbonyl-2-aza-1,3-dienes (2) and (3) from the silylimines (1), and have studied their cycloaddition to electron-rich dienophiles, $\ddagger$  *e.g.* the enamines (4) and (5).

Thus, the reaction of  $(1)^{10}$  with dimethyl acetylenedicarboxylate (toluene; 25 °C; 4 h) gave the azadienes (2) in 94—97% yield after distillation. Fluoride-induced desilylation occurred smoothly; when the diene (2a) was treated with caesium fluoride (MeOH; 25 °C; 15 h) and the resulting mixture distilled, the 2-azadiene (3a) was formed in nearly quantitative yield (Scheme 1; Table 1). In both processes only one stereoisomer was obtained in the crude product.¶

The reactivity of the diene (3a) towards electron-rich alkenes was then investigated. Treatment of (3a) with the pyrrolidine enamines (4) and (5)  $(CH_2Cl_2; 25 \,^{\circ}C; 4 \,h)$  led to a crude product which was chromatographed (basic alumina; toluene–ether, 5:1) or triturated with hexane, respectively, to afford exclusively the *exo*-cycloadducts (6) and (7) in excellent yields\*\* (Scheme 2; Table 2). The regio- and stereo-chemical

assignments were deduced from <sup>1</sup>H n.m.r. (200 MHz) spectral data; thus the appearance of a singlet at  $\delta$  ca. 4.5 assigned to C(1) H clearly shows the C<sub>a</sub>-enamine carbon of the dienophile to be bonded to C(1) of the diene. Nuclear Overhauser enhancement experiments on (7) reveal a cis-fused bicyclic structure in which H(1) and H(4a) are axially oriented in a chair-like conformation.††,‡‡ Acid hydrolysis of (6) (2M-HCl; THF; 50 °C; 2 h) and (7) (2M-HCl; THF; 50 °C; 10 h) resulted in their aromatization [quantitative for (6) and 70% for (7)] to yield the dihydro-2-pyrindine (8) and the tetrahydroisoquinoline (9), respectively.§§



Scheme 1. Reagents: i, MeO<sub>2</sub>CC=CCO<sub>2</sub>Me, toluene, 25 °C, 4 h; ii, (a) CsF-MeOH, 25 °C, 15 h; (b) distillation.

Table 1. Azadienes	(2)	and	(3)	from	sil	ylimines	(1)	).
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Compound <sup>a</sup>	R	Yield <sup>b</sup> (%)	M.p. (°C) or b.p. (°C)/torr
(2a)	Ph	95	$48-50(108/10^{-2})$
(2b)	$p-C1C_6H_4$	97	105—106°
(2c)	p-MeOC <sub>6</sub> H <sub>4</sub>	96	8486°
(2d)	2-Thienyl	96	103/10-2
(2e)	PhCH=CH	94	(Oil) <sup>d</sup>
( <b>3a</b> )	Ph	96	57-59 (105/10 <sup>-2</sup> )

<sup>a</sup> All new compounds reported here gave satisfactory elemental analytical figures. <sup>b</sup> Yields of distilled compounds. <sup>c</sup> Recrystallised from hexane-chloroform. <sup>d</sup> Pure compound; decomposes on column chromatography or when distilled.

 $^{\dagger\dagger}$  Selectivities towards the *exo*-isomers have been found in some 2-azadienes.<sup>8,11</sup>

<sup>‡‡</sup> Despite the presence of a single stereoisomer, further studies to ascertain whether this cycloaddition is concerted are needed.

§§ Compounds (8) and (9) gave the expected spectral data. For example: (8),  $^{13}C$  n.m.r. (20 MHz; CDCl<sub>3</sub>)  $\delta$  166.81 (s), 166.60 (s), 155.72 (s), 154.96 (s), 140.13 (s), 138.35 (s), 128.87 (d), 128.51 (d), 128.15 (d), 52.62 (q), 52.31 (q), 32.61 (t), 32.47 (t), and 24.92 (t).

<sup>&</sup>lt;sup>+</sup> Despite two reports dealing with the synthesis of this type of azadiene, no cycloadditions have been reported.<sup>4</sup>

<sup>&</sup>lt;sup>‡</sup> Cycloaddition of electron-rich olefins with electronically neutral 2-azadienes takes place sluggishly.<sup>8</sup>

<sup>§</sup> The inverse electron demand Diels-Alder reaction of electron-poor 1,2,4-triazines with enamines has been exploited for the synthesis of natural products.<sup>9</sup>

<sup>¶</sup> Structures (2) and (3) were established by spectroscopic means (i.r., mass, <sup>1</sup>H and <sup>13</sup>C n.m.r.); their stereochemistry has not been yet defined. For example: (2a), <sup>13</sup>C n.m.r. (20 Mhz; CDCl<sub>3</sub>)  $\delta$  170.20 (s), 164.30 (s), 163.89 (d), 151.42 (s), 136.46(s), 132.70 (d), 129.83 (d), 129.56 (d), 52.62 (q), 52.00 (q), and 0.41 (q); (3a), <sup>13</sup>C n.m.r. (20 MHz; CDCl<sub>3</sub>)  $\delta$  164.65(s), 163.76 (d), 163.33 (s), 151.74 (s), 134.48 (s), 131.70 (d), 128.69 (d), 128.18 (d), 108.13 (d), 52.36 (q), and 50.87 (q).

<sup>\*\*</sup> Compounds (6) and (7) were characterized by spectroscopic means (i.r., mass, <sup>1</sup>H and <sup>13</sup>C n.m.r.). For example: (7), <sup>1</sup>H n.m.r. (200 MHz; CDCl<sub>3</sub>)  $\delta$  1.25—1.93 (m, 12H), 2.16—2.34 (m, 2H), 2.74—2.88 (m, 2H), 3.25 (t, J 4 Hz, 1H), 3.75 (s, 6H), 4.21 (s, 1H, NH), 4.56 (s, 1H), and 7.26—7.44 (m, 5H, Ar).



Scheme 2. *Reagents:* i, CH<sub>2</sub>Cl<sub>2</sub>, 25 °C, 4 h; ii, 2M-HCl, THF, 50 °C, 2—10 h; iii, (a) CH<sub>2</sub>Cl<sub>2</sub>, 25 °C, 4 h; (b) 2M-HCl, THF, 50 °C, 2 h.

Table 2. Cycloadducts (6)—(9) from 2-azadienes (2a) and (3a), and enamines (4) and (5).

Compound <sup>a</sup>	2-Azadiene	Enamine	Yield <sup>b</sup> (%)	M.p. (°C)
(6)	( <b>3a</b> )	(4)	82(70)	122-124
(7)	( <b>3a</b> )	(5)	95(85)	156
(8)	(2a)	(4)	92(78)	8990
(9)	( <b>2a</b> )	(5)	95(92)	103-105

<sup>a</sup> All new compounds reported here gave satisfactory elemental analytical figures. <sup>b</sup> Yields in parentheses refer to purified compounds; see text.

The trimethylsilyl-substituted azadienes (2) represent useful synthons for the straightforward formation of (8) and (9). Thus, treatment of the diene (2a) with the enamines (4) and (5) (CH<sub>2</sub>Cl<sub>2</sub>; 25 °C; 4 h), hydrolysis of the resulting mixture (2m-HCl; THF; 50 °C; 2 h), and purification of the resulting oily residue by recrystallisation or column chromatography  $(SiO_2; toluene-ether, 2:1)$ , respectively, gave high yields of (8) and (9) (Scheme 2; Table 2).

In conclusion, we have demonstrated the inverse electron demand [4 + 2] cycloaddition of 2-azadienes bearing electronwithdrawing substituents to enamines, leading to the 2-pyrindine and isoquinoline skeletons. The ease with which this type of 2-azadiene is prepared from readily available starting materials, and the high yields obtained in all instances, are noteworthy.

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