

## New Method for the Synthesis of 2-Aza-1,3-Butadienes

Attila Sisak

Research Group for the Petrochemistry of the Hungarian Academy of  
Sciences, Hungary

**Abstract:** 2-Aza-1,3-butadienes have been synthesized from carbonyl compounds and 1,1,1,3,3,3-hexamethyl-disilazane in the presence of cobalt-containing catalysts. The best yields (up to 95%) were achieved in the case of aldehydes branched in the  $\alpha$ -position and 2-methylcyclohexanone. In the case of two  $\alpha,\beta$ -unsaturated ketones, pyridine derivatives were found as the main products.

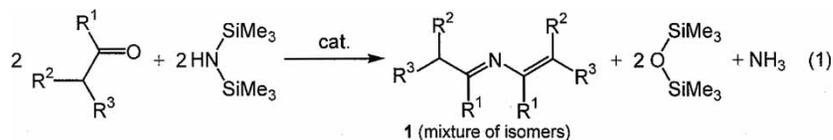
**Keywords:** 2-Aza-1,3-butadienes, pyridine derivatives, carbonyl compounds, 1,1,1,3,3,3-hexamethyl-disilazane, cobalt catalysts

2-Aza-1,3-butadienes are important intermediates of various nitrogen-containing heterocycles.<sup>[1–9]</sup> However, the synthetic routes leading to these substances involve often several reaction steps<sup>[2,3]</sup> and/or the starting materials are hardly accessible.<sup>[3,6,8]</sup>

We have found a simple, one-pot method to prepare a series of alkyl- and aryl-substituted 2-azabutadienes (Chart 1). A carbonyl compound was heated with a slight excess of 1,1,1,3,3,3-hexamethyl-disilazane (HMDSA) at 60–120°C in toluene or without solvent under argon in the presence of an anhydrous Co(II) salt. CoBr<sub>2</sub>, CoI<sub>2</sub>, and an ionic complex of the type [CoB<sub>6</sub>][Co(CO)<sub>4</sub>]<sub>2</sub> (B = base) formed from [Co<sub>2</sub>(CO)<sub>8</sub>] under the reaction conditions<sup>[10,11]</sup> proved the most efficient catalysts, but some other transition-metal compounds were active as well. The products were analyzed by gas chromatography (GC) and the gas chromatography-mass spectrometry (GC-MS) method

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Address correspondence to Attila Sisak, Research Group for the Petrochemistry of the Hungarian Academy of Sciences, H-8201 Veszprém, P.O. Box 158, Hungary. E-mail: sis014@almos.vein.hu



| Product | R <sup>1</sup>                    | R <sup>2</sup> | R <sup>3</sup>      |
|---------|-----------------------------------|----------------|---------------------|
| 1a      | H                                 | Et             | Et                  |
| 1b      | H                                 | Me             | Pr                  |
| 1c      | Me                                | H              | iPr                 |
| 1d      | (CH <sub>2</sub> ) <sub>5</sub>   |                | H                   |
| 1e      | CH(CH <sub>2</sub> ) <sub>4</sub> |                | Me                  |
| 1f      | (CH <sub>2</sub> ) <sub>4</sub>   |                | H                   |
| 1g      | Me                                | H              | CH=CMe <sub>2</sub> |
| 1h      | Me                                | H              | Ph                  |
| 1i      | H                                 | Ph             | Ph                  |
| 1j      | Me                                | H              | CH=CHPh             |

Chart 1.

(Table 1). The isolated new azadienes were characterized also by IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra (Table 2). In the cases of R<sup>2</sup> ≠ R<sup>3</sup>, more isomeric 2-azadienes were formed. Suggested structures of the isolated and characterized isomers of 1 compounds are compiled in Table 3.

Only aldehydes branched in the α-position (R<sup>1</sup> = H, R<sup>2</sup> ≠ H, R<sup>3</sup> ≠ H) gave 1 in good yields; the linear ones led to nonvolatile (presumably polymeric) products. In the case of ketones, by-products such as silyl enol ethers were formed as well (Table 1). Sterically hindered ketones (2-methyl-3-pentanone, campher, etc.) could not be converted under the reaction conditions. Interestingly, 4-phenyl-3-buten-2-one (R<sup>4</sup> = Ph) and 4-(2-furyl)-3-buten-2-one (R<sup>4</sup> = 2-furyl) gave pyridine derivatives (2) as main products (Chart 2, Table 2). From conjugated dicarbonyl compounds (2,4-pentanedione, ethyl 3-oxobutanoate), silyl enol ethers were formed; a nonconjugated diketone, 2,5-hexanedione, however, provided the ring-closure product 2,5-dimethyl-pyrrol (cf. Ref. [14]).

Corriu and coworkers [3] prepared 2-azadienes and pyridine derivatives starting from *N,N*-bis(trimethylsilyl) enamines and carbonyl compounds in the presence of catalytic amounts of bases such as F<sup>-</sup>. Under our reaction conditions, *N,N*-bis(trimethylsilyl) enamines may be formed as intermediates catalyzed by Co-complexes (Scheme 1). In the second step, the intermediate reacts with a second molecule of aldehyde or ketone leading to 1 analogous to that proposed by Corriu and his coworkers. In the case of

**Table 1.** Products of the cobalt-catalyzed reaction of carbonyl compounds and HMDSA<sup>a</sup>

| Substrate (conversion)                      | 2-Aza-1,3-butadiene<br>(selectivity [w/w%] <sup>b</sup> /[ratio<br>of the isomers found] <sup>c</sup> ) | Other products <sup>c</sup>  |
|---|---|--|
| 2-Ethyl-butanal (100)                       | <b>1a</b> (95 <sup>d</sup> /[1.0])  | <sup>e</sup>   |
| 2-Methyl-pentanal (100) <sup>f,g</sup>      | <b>1b</b> (93 <sup>d</sup> /[0.38:0.62])  | <sup>e</sup>   |
| Pentanal (100)                              | <1  | Nonvolatile products   |
| 4-Methyl-2-pentanone (100)                  | <b>1c</b> (27/[0.68:0.21:0.11])   | Silyl enol ether (main product)  |
| 2-Methyl-3-pentanone (<1)                   | —   | —  |
| Cyclohexanone (13) <sup>h</sup>             | <b>1d</b> (95/[1.0])  | <sup>e</sup>   |
| Cyclohexanone (96) <sup>f,g</sup>           | <b>1d</b> (32 <sup>d</sup> /[1.0])  | Silyl enol ether, dehydrated aldol dimer, unknown main product ( $M^+ = 274$ $m/z$ ) |
| 2-Methyl-cyclohexanone (90) <sup>f</sup>    | <b>1e</b> (82 <sup>d</sup> /[0.07:0.62:0.11:0.20])  | Silyl enol ether, silyl alkyl ether  |
| Cyclopentanone (100) <sup>f</sup>           | <b>1f</b> (16/[1.0])  | Dehydrated aldol dimer, nonvolatile products   |
| 2,4-Pentanedione (100)                      | <1  | Silyl enol ether (main product), nonvolatile products                                |
| 2,5-Hexanedione (81) <sup>f,g</sup>         | <1  | 2,5-Dimethylpyrrole (main product)   |
| 4-Methyl-3-penten-2-one (32) <sup>f</sup>   | <b>1g</b> (17/[1.0])  | Silyl enol ether (main product)  |
| Ethyl 3-oxo-butanoate (88) <sup>f</sup>     | <1  | Ethyl 3-amino-2-butenolate, silyl enol ether (main product)                          |
| Acetophenone (35)                           | <b>1h</b> (24/[0.32:0.68])  | Silyl enol ether (main product), dehydrated aldol dimer, uncharacterized products    |
| Diphenyl-acetaldehyde (98) <sup>f</sup>     | <b>1i</b> (75 <sup>d</sup> /[1.0])  | Silyl enol ether, uncharacterized products   |
| 4-Phenyl-3-buten-2-one (95)                 | <b>1j</b> (8/[0.58:0.42])   | <b>2a</b> (main product), silyl enol ether, uncharacterized products                 |
| 4-(2-Furyl)-3-buten-2-one (85) <sup>f</sup> | <1  | <b>2b</b> (main product), silyl enol ether, uncharacterized products                 |

<sup>a</sup>[Carbonyl compound]:[HMDSA]=1:1, 5 mol% [Co<sub>2</sub>(CO)<sub>8</sub>] catalyst, 110°C, CO atmosphere, toluene solvent, unless otherwise stated.

<sup>b</sup>Based on GC analysis unless otherwise stated.

<sup>c</sup>Based on GC-MS analysis.

<sup>d</sup>Isolated yield.

<sup>e</sup>Not determined.

<sup>f</sup>5 mol% anhydrous CoBr<sub>2</sub> catalyst.

<sup>g</sup>No solvent.

<sup>h</sup>7 mol% Bu<sub>4</sub>N[Co(CO)<sub>4</sub>] catalyst.

**Table 2.** Properties of the products **1** and **2**

| Product  | Bp <sup>a</sup> , Mp (°C) | MS ( <i>m/z</i> )   | IR (CH <sub>2</sub> Cl <sub>2</sub> ,<br>ν(C=C),<br>cm <sup>-1</sup> ) | <sup>1</sup> H NMR (CDCl <sub>3</sub> , δ, ppm)   | <sup>13</sup> C NMR (CDCl <sub>3</sub> , δ,<br>ppm)                              |
|--|---------------------------|---|--|---|--|
| <b>1a</b> (R <sup>1</sup> = H,<br>R <sup>2</sup> = R <sup>3</sup> = Et)      | 90–91 <sup>10</sup>       | 181 ( <i>M</i> <sup>+</sup> ), 152, 110 (base<br>peak), 55, 41  | 1625   | 0.88 (6 H, t, <i>J</i> = 7.4 Hz), 1.02 (3 H, t,<br><i>J</i> = 7.4 Hz), 1.04 (3 H, t,<br><i>J</i> = 7.4 Hz), 1.50 (4 H, quintet,<br><i>J</i> = 7.4 Hz), 2.1 (1 H, m), 2.20 (2 H,<br><i>J</i> = 7.4 Hz), 2.48 (2 H, q,<br><i>J</i> = 7.4 Hz), 6.37 (1 H, s), 7.37 (1H,<br>d, <i>J</i> = 6.6 Hz) | 11.46, 12.57, 13.04,<br>22.59, 24.90, 26.62,<br>47.73, 135.88, 142.94,<br>166.10 |
| <b>1b</b> (R <sup>1</sup> = H,<br>R <sup>2</sup> = Me, R <sup>3</sup> = Pr)  | 91–94 <sup>10 b</sup>     | 181 ( <i>M</i> <sup>+</sup> ), 110, 82, 55<br>(base peak), 41   | 1624   | 0.8–1.0 (6 H, m), 1.04 (3 H, m), 1.1–<br>1.8 (6 H, m), 1.81 (3 H, s), 2.01 (2 H,<br>m), 2.36 (1 H, m), 6.35 (1 H, s,<br>broad), 7.37 (1 H, m) <sup>c</sup>  |  |
| <b>1c</b> (R <sup>1</sup> = Me,<br>R <sup>2</sup> = H, R <sup>3</sup> = iPr) | 65–74 <sup>3 d</sup>      | 181 ( <i>M</i> <sup>+</sup> ), 166 (base<br>peak), 138, 124, 41 | 1618   | 0.86 (6 H, d, <i>J</i> = 6.5), 0.90 (6 H, d,<br><i>J</i> = 6.6), 1.86 (1 H, m), 1.97 (2 H, d,<br><i>J</i> = 7.2), 2.08 (3 H, s), 2.10 (1 H,<br>octet, <i>J</i> = 6.6), 2.26 (2 H, d,<br><i>J</i> = 6.6), 5.99 (1 H, s, broad) <sup>e</sup>  |  |

|  |                      |  |      |  |
|--|----------------------|--|------|--|
| <b>1d</b> ( $R^1 + R^2 =$<br>( $\text{CH}_2$ ) <sub>5</sub> , $R^3 = \text{H}$ ) <sup>f</sup>                              | 108–111 <sup>5</sup> | 177 ( $M^+$ , base peak),<br>134, 81, 79, 41           | 1621 | 1.55–1.75 (6 H, m), 1.86 (4 H, m),<br>2.12 (4 H, m), 2.35 (4 H, m), 5.3 (1<br>H, t, $J = 3.8$ Hz)            |
| <b>1e</b> ( $R^1 + R^2 =$<br>$\text{CH}(\text{CH}_2)_4$ ,<br>$R^2 = \text{Me}$ )   | 93–96 <sup>3</sup>   | 205 ( $M^+$ ), 191, 162 (base<br>peak), 148, 41        | 1630 | 1.11 (3 H, d, $J = 7.3$ Hz), 1.2–2.5 (17<br>H, m), 1.39 (3 H, s, broad) <sup>e</sup>                         |
| <b>1f</b> ( $R^1 + R^2 =$<br>( $\text{CH}_2$ ) <sub>4</sub> , $R^3 = \text{H}$ ) <sup>g</sup>                              |                      | 149 ( $M^+$ ), 148 (base<br>peak), 162, 120, 91,<br>41 |      |  |
| <b>1g</b> ( $R^1 = \text{Me}$ ,<br>$R^2 = \text{H}$ ,<br>$R^3 = \text{CH} = \text{CMe}_2$ )                                | 71–80 <sup>3 d</sup> | 177 ( $M^+$ ), 149, 81 (base<br>peak), 79, 41          | 1626 | 1.85 (9 H, s, broad), 2.15 (9, H, s,<br>broad), 6.03 (2 H, s, broad), 6.49 (1<br>H, s), 7.20 (1 H, s)        |
| <b>1h</b> ( $R^1 = \text{Me}$ ,<br>$R^2 = \text{H}$ , $R^3 = \text{Ph}$ ) <sup>g</sup>                                     |                      | 221 ( $M^+$ ), 115, 91, 77<br>(base peak), 51          |      |  |
| <b>1i</b> ( $R^1 = \text{H}$ , $R^2 = \text{Ph}$ ,<br>$R^3 = \text{Ph}$ )  | 176 (mp)             |  | 1641 | 6.95 (1 H, d, $J = 11.7$ ), 7.1–7.6 (20 H,<br>m), 8.08 (1 H, s), 8.42 (1 H, d,<br>$J = 11.7$ )               |
|  |                      |  |      | 77.20, 119.85, 126.75,<br>127.13, 128.14,<br>128.38, 129.37,<br>129.69, 129.80,<br>136.94, 157.93,<br>162.12 |
| <b>1j</b> ( $R^1 = \text{Me}$ , $R^2 = \text{H}$ ,<br>$R^3 = \textit{trans}$ -<br>$\text{CH} = \text{CHPh}$ ) <sup>g</sup> |                      | 273 ( $M^+$ , base peak),<br>272, 196, 169, 91         |      |  |

(continued)

**Table 2.** Continued

| Product   | Bp <sup>a</sup> , Mp (°C) | MS ( <i>m/z</i> )  | IR (CH <sub>2</sub> Cl <sub>2</sub> ,<br>ν(C=C),<br>cm <sup>-1</sup> ) | <sup>1</sup> H NMR (CDCl <sub>3</sub> , δ, ppm)                  | <sup>13</sup> C NMR (CDCl <sub>3</sub> , δ,<br>ppm)   |
|---|---------------------------|--|--|--|---|
| <b>2a</b> (R <sup>4</sup> = Ph)                   | 120–135 <sup>0.1 g</sup>  | 271 ( <i>M</i> <sup>+</sup> ), 270 (base peak), 194, 127, 77 | 1632   | 2.38 (3 H, s), 6.73 (1 H, d, <i>J</i> = 16.6), 7.1–7.7 (13 H, m) | 27.43, 117.32, 120.05, 125.46, 127.04, 127.74, 128.07, 128.25, 128.66, 128.78, 130.46, 137.21, 138.75, 149.33, 155.72, 158.68 |
| <b>2b</b> (R <sup>4</sup> = 2-furyl) <sup>g</sup> |                           | 251 ( <i>M</i> <sup>+</sup> ), 223, 197 (base peak), 83, 63  |  |  |   |

<sup>a</sup>Pressure in mm Hg, 1 mm Hg = 133.32 Pa.

<sup>b</sup>Bp: 89<sup>8.5</sup>.<sup>[12]</sup>

<sup>c</sup>Mixture of two isomers.

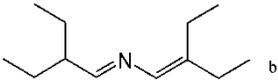
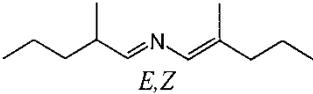
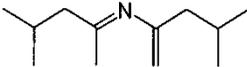
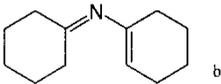
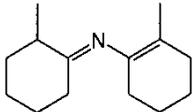
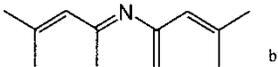
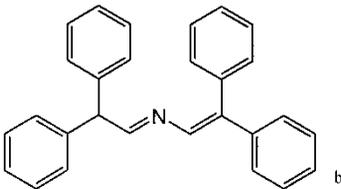
<sup>d</sup>The fraction was further purified by chromatography (see text).

<sup>e</sup>Major Isomer.

<sup>f</sup>See ref. [13].

<sup>g</sup>Not isolated.

**Table 3.** Suggested structures of the isolated and characterized isomers of **1** compounds<sup>a</sup>

| 2-Aza-1,3-butadiene | Structure   |
|---------------------|---|
| 1a                  |    |
| 1b                  |    |
| 1c                  |    |
| 1d                  |    |
| 1e                  |   |
| 1g                  |  |
| 1i                  |  |

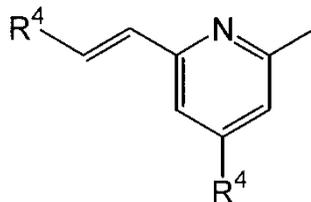
<sup>a</sup>Cf. Tables 1 and 2.<sup>b</sup>Only isomer found.

some  $\alpha,\beta$ -unsaturated carbonyl compounds, ring closure of **1** and subsequent dehydrogenation takes place, presumably, resulting in **2** (cf. Ref. [3]).

## EXPERIMENTAL

### General

All manipulations involving air-sensitive compounds were carried out by the usual Schlenk technique using deoxygenated, dry solvents and gases as well as



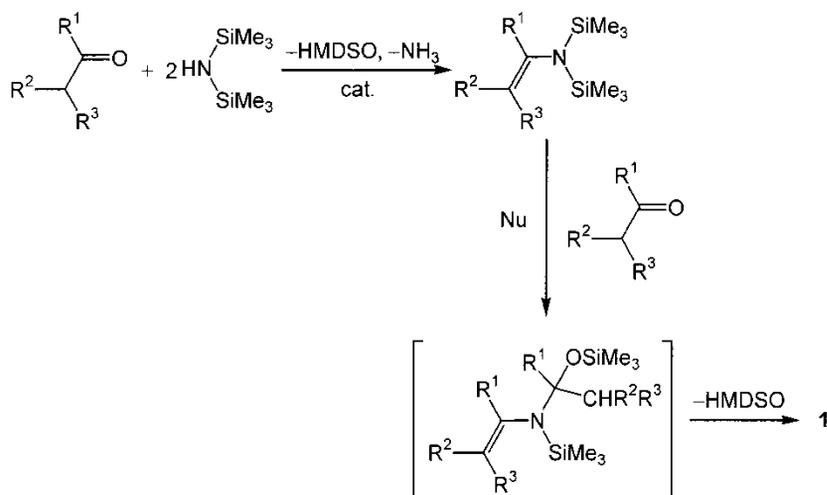
**2a:** R<sup>4</sup> = Ph, **2b:** R<sup>4</sup> = 2-furyl

*Chart 2.*

reaction vessels with magnetic stirring. Gas chromatograms were recorded on a Hewlett-Packard model 5830 A chromatograph (with FID), and GC-MS analyses were performed on a Hewlett-Packard 5890 series II GC-MSD equipment using SPB1 (Supelco) capillary columns (30 m). Infrared spectra were recorded by using a 0.06 to 0.12-mm CaF<sub>2</sub> cuvette on Specord M 80 (Carl Zeiss, Germany). <sup>1</sup>H and NMR <sup>13</sup>C NMR spectra were obtained on a Varian Unity 300 spectrometer.

### Synthesis of **1**

In a typical procedure, 0.44 g (2.0 mmol) of CoBr<sub>2</sub>, 2.5 ml (20.0 mmol) 2-methylpentanal, and 4.6 ml (22.0 mmol) of HMDSA were heated



*Scheme 1.*

gradually to 110°C. Evolution of ammonia gas indicated the beginning of the reaction. The mixture was stirred for 6 h at 110°C. GC and GC-MS analysis showed the quantitative conversion of 2-methylpentanal and the formation of two isomers of **1b** (Tables 1 and 2). The mixture of the two isomers was isolated by distillation in vacuo in 91% yield (cf. Ref. [10]).

### Synthesis of 2a

The procedure was modified so that 0.34 g (1.0 mmol) of  $\text{Co}_2(\text{CO})_8$ , 2.9 g (20 mmol) of 4-phenyl-3-buten-2-one, and 4.6 ml (22.0 mmol) of HMDSA were heated in toluene (10 ml) at 120°C under a CO atmosphere for 6 h. The reaction mixture was filtered, the solvent removed in vacuo, and the residue fractionated. On the basis of GC-MS analysis (see Table 2), the second fraction (120–135°C) at 0.1 mmHg pressure; 1 mm Hg = 133.32 Pa) contained mostly **2a**. This fraction was purified by thin-layer chromatography (TLC) using a silica-gel plate and a 9:1  $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$  mixture as eluant. Compound **2a** was isolated as a pale yellow oil in 43% yield.

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