

## Addition of Primary Amines to Conjugated Allenyl Aldehydes and Ketones

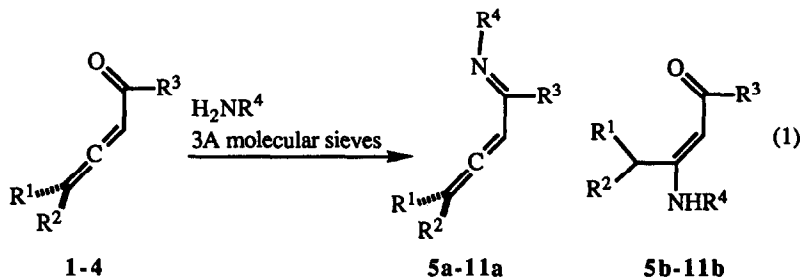
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**Abstract:** *Allenyl imines have been prepared by condensation of allenyl aldehydes with primary amines.*

Conjugated allenyl ketones and aldehydes have been found to be useful in a variety of synthetic transformations.<sup>1</sup> In contrast, conjugated allenyl imines are virtually unknown despite their potential applications in organic synthesis and implicated involvement as inhibitors of pyridoxal phosphate dependent enzymes.<sup>2</sup> Under standard conditions for imine formation conjugated allenyl ketones have been reported to undergo exclusively 1,4-addition to give allenylvinyl ketones.<sup>3</sup> Herein we report the synthesis of some allenyl imines derived from conjugated allenyl aldehydes.

To direct the chemistry toward imine formation versus conjugate addition it was thought that the polarity and hydrogen bonding nature of the solvent would effect the relative rates of 1,4 versus 1,2-addition (eq 1).



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Solvent	fraction a <sup>4</sup>	fraction b		
1	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>3</sub> C	H	5	(CH <sub>3</sub> ) <sub>3</sub> C	CH <sub>3</sub> OH	1	0	
						THF	1	0	
						CH <sub>2</sub> Cl <sub>2</sub>	1	0	
						C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	1	0	
						CCl <sub>4</sub>	1	0	
						6	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub>	1	0
						7	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	1	0
						8	C <sub>6</sub> H <sub>5</sub>	.73	.17
2			CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>3</sub> C	CH <sub>2</sub> Cl <sub>2</sub>	0			
3	CH <sub>3</sub>	CH <sub>3</sub>	H	9	(CH <sub>3</sub> ) <sub>3</sub> C	CH <sub>2</sub> Cl <sub>2</sub>	.97	.03	
						CH <sub>3</sub> OH	.98	.02	
						THF	.99	.01	
						CH <sub>2</sub> Cl <sub>2</sub>	.85	.15	
						C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	.86	.14	
						CCl <sub>4</sub>	0	1	
4				10	C <sub>6</sub> H <sub>5</sub>	0	1		
			CH <sub>3</sub>	11	(CH <sub>3</sub> ) <sub>3</sub> C	0	1		

However, it was found that the substituents on the allene terminal positions played a crucial role in determining the success of the reaction. Surprisingly, aldehyde 1 gave imine 5a in a wide variety of polar and nonpolar

solvents. Only imines **6a** - **7a** were formed in the polarizable nonpolar solvent  $\text{CCl}_4$ . Similar yields (73 - 94%) were obtained in  $\text{CH}_2\text{Cl}_2$ . Aniline too gave the imine (**8a**) as the major product and a significant amount of vinyamine (**8b**). For allenyl aldehyde **3** the reaction with *t*-butylamine in all solvents studied gave predominantly imine **9a** with varying amounts of vinyamine **9b**. Higher selectivity and better yields were obtained in  $\text{CH}_2\text{Cl}_2$ . In contrast to **1**, **3** reacted with amines **6** - **9** to give some (30 - 40 %) of the corresponding imine and a complex mixture of products. Lowering the reaction temperature slowed the rate of amine addition but had no effect on the distribution of products. For these examples isolation of the imine failed. Apparently with **3** *t*-butylamine has sufficient steric bulk to obviate side reactions. Aniline gave exclusively 1,4-addition (**10b**) when reacting with **3**. Allenyl ketone **2** gave no addition of *t*-butylamine under the standard reaction conditions (vide infra), while **4** gave only the vinyamine **11b**.

Reactions were conducted under a dry argon atmosphere using standard Schlenk techniques. All amines were filtered through basic alumina immediately prior to use. In a typical reaction, 96.5 mg (1.33 mmol) of butylamine diluted in 5 mL of  $\text{CH}_2\text{Cl}_2$  was added slowly to a stirring solution of 184 mg (1.33 mmol) of **1**, 10 mL of  $\text{CH}_2\text{Cl}_2$  and molecular sieves. After stirring for two hours at 22 °C, the reaction mixture was filtered through Celite and the solvent removed by a rotary evaporator. Bulb to bulb distillation (45 °C,  $10^{-5}$  mm Hg) gave **6a** 242 mg (94%) as a colorless oil.<sup>4</sup>

## References

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- (a) Tamnefors I.; Claesson, A.; Karlsson, M. *Acta Pharm. Suec.* **1975**, *12*, 435. (b) Bol'shedvorskaya, R. L.; Pavlova, G. A.; Garrilov, L. D.; Alekseeva, N. V.; Vereshchagin, L. I. *J. Org. Chem. USSR*, **1972**, *8*, 1927.
- Fraction of imine **a** and aminovinyketone **b** products by  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ ). Isolated yields of major products were from (73 - 95%). **5a**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  1.03, (s, 9H), 1.16 (s, 9H), 1.71 (d,  $J = 2.8$  Hz, 3H), 5.84 (dq,  $J = 2.8, 8.7$  Hz, 1H), 7.64 (d,  $J = 8.7$ , 1H);  $^{13}\text{C}\{^1\text{H}\}$  (75 MHz:  $\text{CDCl}_3$ )  $\delta$  14.48, 29.00, 29.67, 33.63, 56.81, 95.77, 111.66, 155.37, 209.00; IR (neat) 1947 ( $\text{C}=\text{C}=\text{C}$ ), 1628 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$ ; MS  $m/z$  ( $\text{M}^+$ ) 193; HRMS  $m/z$  for  $\text{C}_{13}\text{H}_{23}\text{N}$  calcd 193.1830, found 193.1849. **6a**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  0.78 (t,  $J = 7.3$  Hz, 3H), 0.94 (s, 9H), 1.20 (hex,  $J = 7.0, 2\text{H}$ ), 1.45 (pent,  $J = 7.0, 2\text{H}$ ), 1.61 (d,  $J = 1.8, 3\text{H}$ ), 3.26 (t,  $J = 7.0, 2\text{H}$ ), 5.73 (dq,  $J = 1.8, 7.7$  Hz, 1H), 7.56 (d,  $J = 7.7$  Hz, 1H);  $^{13}\text{C}\{^1\text{H}\}$  (75 MHz:  $\text{CDCl}_3$ )  $\delta$  13.63, 14.23, 20.16, 28.64, 32.82, 33.37, 60.77, 94.85, 11.46, 160.02, 208.84; IR (neat) 1947 ( $\text{C}=\text{C}=\text{C}$ ), 1633 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$ ; MS  $m/z$  ( $\text{M}^+$ ) 193 HRMS  $m/z$  for  $\text{C}_{13}\text{H}_{23}\text{N}$  calcd 193.1830, found 193.1836. **7a**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  1.10 (s, 9H), 1.76 (d,  $J = 2.8, 3\text{H}$ ), 4.59 (s, 2H), 5.98 (dq,  $J = 2.8, 8.9, 1\text{H}$ ), 7.26 (m, 5H), 7.86 (d,  $J = 8.9$  Hz, 1H);  $^{13}\text{C}\{^1\text{H}\}$  (75 MHz:  $\text{CDCl}_3$ )  $\delta$  14.22, 28.68, 33.37, 64.76, 94.87, 111.66, 126.60, 127.64, 128.17, 139.15, 161.20, 209.24; IR (neat) 1947 ( $\text{C}=\text{C}=\text{C}$ ), 1631 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$ ; MS  $m/z$  ( $\text{M}^+$ ) 227. HRMS  $m/z$  for  $\text{C}_{16}\text{H}_{21}\text{N}$  calcd 227.1574, found 227.1664. **8a**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  1.10 (s, 9H), 1.80 (d,  $J = 2.7, 3\text{H}$ ), 6.11 (dq,  $J = 2.7, 9.0, 1\text{H}$ ), 7.23 (m, 5H), 7.94 (d,  $J = 9.0$  Hz, 1H);  $^{13}\text{C}\{^1\text{H}\}$  (75 MHz:  $\text{CDCl}_3$ )  $\delta$  14.46, 29.02, 33.87, 96.14, 112.50, 120.87, 125.60, 129.02, 152.04, 160.62, 211.30; IR (neat) 1943 ( $\text{C}=\text{C}=\text{C}$ ), 1613 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$ ; MS  $m/z$  ( $\text{M}^+$ ) 213. HRMS  $m/z$  for  $\text{C}_{15}\text{H}_{19}\text{N}$  calcd 213.1517, found 213.1503. **9a**  $^1\text{H}$  NMR (200 MHz:  $\text{CDCl}_3$ )  $\delta$  1.17, (s, 9H), 1.73 (d,  $J = 2.9$  Hz, 6H), 5.80 (dq,  $J = 2.9$  Hz, 8.8 Hz, 1H), 7.68 (d,  $J = 8.8$  Hz, 1H);  $^{13}\text{C}\{^1\text{H}\}$  (50 MHz:  $\text{CDCl}_3$ )  $\delta$  19.97, 29.64, 56.97, 94.00, 98.31, 155.07, 210.12; IR ( $\text{CDCl}_3$ ) 1953 ( $\text{C}=\text{C}=\text{C}$ ), 1621 ( $\text{C}=\text{N}$ )  $\text{cm}^{-1}$ ; MS  $m/z$  ( $\text{M}^+$ ) 151. HRMS  $m/z$  for  $\text{C}_{10}\text{H}_{17}\text{N}$  calcd 151.1361 found 151.1343. **10b**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  1.06 (d,  $J = 6.9, 6\text{H}$ ), 2.82 (hept,  $J = 6.9, 1\text{H}$ ), 5.07 (d,  $J = 8.3, 1\text{H}$ ), 6.82 (d,  $J = 8.3, 1\text{H}$ ), 6.92 (m, 2H), 7.28 (m, 3H); IR ( $\text{CDCl}_3$ ) 1640  $\text{cm}^{-1}$ . **11b**  $^1\text{H}$  NMR (300 MHz:  $\text{CDCl}_3$ )  $\delta$  1.14 (d,  $J = 7.0, 6\text{H}$ ), 1.39 (s, 9H), 1.98 (s, 3H), 2.95 (hept,  $J = 7.0, 1\text{H}$ ), 4.92 (s, 1H); IR ( $\text{CDCl}_3$ ) 1600  $\text{cm}^{-1}$ .