One-Pot Synthesis of *N*-((Trimethylsilyl)methyl)imines and (Trimethylsilyl)methyl-Substituted Heterocumulenes from (Trimethylsilyl)methyl Azide

Otohiko Tsuge,* Shuji Kanemasa, and Koyo Matsuda

Research Institute of Industrial Science and Department of Molecular Science and Technology, Interdisciplinary Graduate School of Engineering Science, Kyushu University, Kasugakoen, Kasuga 816, Japan

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The reactions of ((trimethylsilyl)methyl)iminotriphenylphosphorane, prepared in situ from (trimethylsilyl)methyl azide and triphenylphosphine, with carbonyl compounds and with heterocumulenes such as carbon dioxide, carbon disulfide, isocyanates, isothiocyanates, and a ketene provide convenient one-pot syntheses of the corresponding *N*-((trimethylsilyl)methyl)imines and (trimethylsilyl)methyl-substituted heterocumulenes, which are versatile reagents for the synthesis of heterocyclic compounds.

N-((Trimethylsilyl)methyl)imines and heterocumulenes bearing a (trimethylsilyl)methyl group adjacent to the cumulene moiety (abbreviated as TMSM-heterocumulenes) are useful reagents in the field of heterocyclic synthesis. The only derivative of *N*-((trimethylsilyl)methyl)imine reported to date, *N*-benzylidene(trimethylsilyl)methylamine,[1] has been found to be a useful precursor for the nonstabilized azomethine ylide 1,3-dipole[2] and the azaallyl anion,[3] whose reactions lead to the formation of five-membered nitrogen heterocycles. The TMSM-heterocumulenes, (trimethylsilyl)methyl isothiocyanate[4] and azide,[5] are also versatile synthetic reagents, but only these and the isocyanate[6] and ketene[7] have been reported.

In addition, it is known that reaction of azides with tertiary phosphines gives iminophosphoranes,[8] and that the latter are useful intermediates for the synthesis of a variety of nitrogen compounds.[9,10]

We have reported a high-yield synthesis of thermally stable (trimethylsilyl)methyl azide (**1**).[5] Thus a new route for the synthesis of *N*-((trimethylsilyl)methyl) compounds may be opened from **1** via the corresponding iminophosphoranes. In the present paper we describe a convenient one-pot synthesis of various *N*-((trimethylsilyl)methyl)imines and TMSM-heterocumulenes from **1**.

***N*-((Trimethylsilyl)methyl)imines.** The reaction of **1** with triphenylphosphine (**2a**) in dry benzene under reflux for 1 h gave ((trimethylsilyl)methyl)iminotriphenylphosphorane (**3a**) in a quantitative yield. Similarly, the trialkoxyiminophosphoranes **3b** and **3c** were obtained in the reactions of **1** with trimethyl phosphite (**2b**) and triethyl phosphite (**2c**) under the same conditions. The iminophosphoranes **3** are stable enough to be purified by distillation.

$$\underset{\mathbf{1}}{Me_3SiCH_2N_3} + \underset{\mathbf{2}}{R_3P} \rightarrow \underset{\mathbf{3}}{Me_3SiCH_2N{=}PR_3}$$

a, R = Ph; **b**, R = OMe; **c**, R = OEt

Iminophosphornanes **3a-c** were each allowed to react with 1 equiv of benzaldehyde (**4a**) at reflux in dry benzene under nitrogen to give *N*-benzylidene(trimethylsilyl)methylamine (**5a**) in good yields (75% from **3a**, 57% from **3b**, 67% from **3c**). Aromatic **4a-c**, heteroaromatic **4d-e**,

$$\underset{\mathbf{1}}{Me_3SiCH_2N_3} + \underset{\mathbf{2a}}{Ph_3P} + \underset{\mathbf{4}}{R^1COR^2} \rightarrow \underset{\mathbf{5}}{Me_3SiCH_2N{=}CR^1R^2}$$

aliphatic **4f,g**, and α,β-unsaturated aldehydes **4h,i** gave the corresponding *N*-((trimethylsilyl)methyl)imines **5a-i** in fair to good yields. Since the condensation with ketones was rather sluggish, acetone was used as a solvent as well as reagent, and the reaction with cyclohexanone was carried out in toluene under reflux for a long time.

The reaction conditions, yields, and boiling points of **5** are summarized in Table I.

NMR spectral data indicate that some of **5** exist as equilibrium mixtures of *E* and *Z* forms in deuteriochloroform at room temperature. The NMR spectral data and *E*/*Z* ratios of **5** are summarized in Table II.

The major components were assigned the *E* form on the basis of the fact that, in an *E*,*Z* isomerism of imines, a bulkier substituent on the imine carbon prefers the position trans to a substituent on the imine nitrogen.[11]

TMSM-Heterocumulenes. We investigated the synthesis of (trimethylsilyl)methyl isocyanate (**6**) and isothiocyanate (**7**) from **1** via the iminophosphorane **3a**. Two methods for the synthesis of **6** have been reported: (1) the reaction of (chloromethyl)trimethylsilane with potassium cyanate in dimethylformamide at 145-150 °C,[6a] and (2) the thermolysis of 1,1-diphenyl-3-((trimethylsilyl)methyl)urea at 250-300 °C.[6b] Isothiocyanate **7** has been prepared by the reaction of (trimethylsilyl)methyl isocyanide with sulfur in refluxing benzene for a long time.[4]

We have now found convenient one-pot syntheses for the isocyanate **6** and isothiocyanate **7**. The reaction of the

$$\underset{\mathbf{1}}{Me_3SiCH_2N_3} + \underset{\mathbf{2a}}{Ph_3P} + CX_2 \rightarrow \underset{\mathbf{6},\ X = O;\ \mathbf{7},\ X = S}{Me_3SiCH_2NCX}$$

(1) Popowski, M.; Böttcher, M.; Kelling, H. *Z. Chem.* **1975**, *15*, 353.
(2) (a) Achiwa, K.; Sekiya, M. *Chem. Lett.* **1981**, 1213. (b) Achiwa, K.; Seikya, M. *Tetrahedron Lett.* **1982**, *23*, 2589. (c) Achiwa, K.; Motoyama, T.; Sekiya, M. *Chem. Pharm. Bull.* **1983**, *31*, 3939. (d) Smith, R.; Livinghouse, T. *J. Org. Chem.* **1983**, *48*, 1554.
(3) We have recently found that fluoride ion induced desilylation of *N*-((trimethylsilyl)methyl)imines generates 2-azaallyl anions which can be captured as adducts to electron-deficient olefins or aldehydes. The results will be published in the near future.
(4) Hirao, T.; Yamada, A.; Hayashi, K.; Ohshiro, Y.; Agawa, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1163.
(5) Tsuge, O.; Kanemasa, S.; Matsuda, K. *Chem. Lett.* **1983**, 1131.
(6) (a) Kozyukov, V. P.; Sheludyakov, V. D.; Mironov, V. F. *Zh. Obshch. Khim* **1968**, *38*, 1179. (b) Smetankina, N. P.; Miryan, N. I. *Ibid.* **1967**, *37*, 1383.
(7) Brady, W. T.; Cheng, T. C. *J. Org. Chem.* **1977**, *42*, 732.
(8) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.
(9) Horner, L.; Gross, A. *Liebigs Ann. Chem.* **1955**, *591*, 117.
(10) Messmer, A.; Pinter, I.; Szego, F. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 228.
(11) Bjorgo, J.; Boyd, D. R.; Watson, C. G. *J. Chem. Soc. Perkin Trans. 2* **1974**, 757. See also the references cited therein.

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Table I. One-Pot Synthesis of *N*-((Trimethylsilyl)methyl)imines 5

5	R^1	R^2	conditions[a] solvent	time, h	yield, %	bp, °C (mmHg)
5a	H	Ph	benzene	2	89	100–103 (22)[b]
5b	H	*p*-ClC_6H_4	benzene	2	84	128–132 (23)
5c	H	*p*-$MeOC_6H_4$	benzene	2	68	140–145 (23)
5d	H	2-furyl	THF	2	75	82–86 (20)
5e	H	2-pyridyl	benzene	2	63	101–105 (22)
5f	H	CMe_3	THF	2	47	56–60 (21)
5g	H	Pr	benzene	12	46	50–54 (22)
5h	H	PhCH=CH (t)	benzene	12	75	80–83 (12)
5i	H	MeCH=CH (t)	benzene	12	63	60–63 (32)
5j	Me	Me	acetone	24	49	50–54 (65)
5k	$-(CH_2)_5-$		toluene	20	64	71–75 (18)

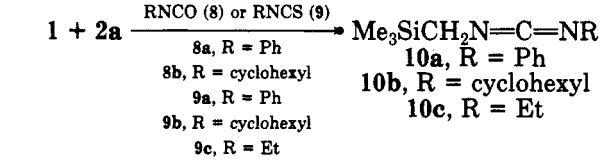
[a] All the reactions were carried out under reflux except for **5g** (at room temperature). [b] Reported bp 75 °C (3 mmHg).[2c]

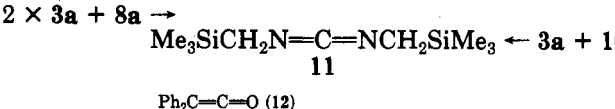
iminophosphorane **3a**, which was prepared from **1** and **2a** in dry tetrahydrofuran, with dry ice under cooling, afforded **6** in 68% yield. Isothiocyanate **7** was formed in 94% yield by the reaction of **1** with **2a** in dry carbon disulfide at room temperature. Our methods are superior to the reported ones[4,6] in terms of simple procedure, mild conditions, and high yields.

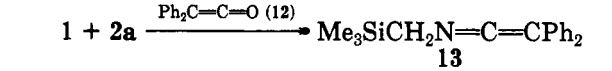
N-((Trimethylsilyl)methyl)carbodiimides have not been reported, and we next investigated the one-pot synthesis of these carbodiimides. Refluxing a benzene solution of iminophosphorane **3a** with 1 equiv of phenyl isocyanate (**8a**) or cyclohexyl isocyanate (**8b**) for 1 h gave *N*-phenyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10a**) or *N*-cyclohexyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10b**); in both reactions the product was a mixture with *N,N'*-bis((trimethylsilyl)methyl)carbodiimide (**11**) (about 5:1 ratio). Carbodiimides **10a** and **10b** could be easily separated from **11** by distillation. Although the same reaction with propyl isocyanate also gave a mixture of *N*-propyl-*N'*-((trimethylsilyl)methyl)carbodiimide and **11**, the boiling points of these were so close that attempted isolation of the *N*-propylcarbodiimide was unsuccessful.

The formation of the byproduct **11** can be attributed to the reaction of the initially formed carbodiimide **10a** or **10b** with iminophosphorane **3a**: the reactions of the isocyanate **8a** with 2 equiv of the iminophosphorane **3a** and of the carbodiimide **10a** with **3a** in benzene under reflux gave **11** in quantitative yields (Scheme I). This result

Scheme I







implies that the reactivity of **8** with **3a** is not high.

However, the formation of **11** could be suppressed by using isothiocyanates **9** in place of isocyanates **8**. The reaction of the iminophosphorane **3a** with phenyl isothiocyanate (**9a**), cyclohexyl isothiocyanate (**9b**), or ethyl isothiocyanate (**9c**) in benzene under reflux gave **10a**, **10b**, or *N*-ethyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10c**) as the sole product in excellent yield.

Finally, the one-pot reaction of the iminophosphorane **3a** with diphenylketene (**12**) in dry benzene under similar conditions was shown to give ketimine **13** in excellent yield.

Experimental Section

General Methods. IR spectra were taken with a JASCO A-702 spectrometer. ^1H NMR spectra were recorded on a Hitachi R-40 or a JEOL FX-100 instrument, and ^{13}C NMR spectra were measured on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. Mass spectra were taken with a JEOL JMS-01SG-2 spectrometer at 75 eV ionization energy. Elemental analyses were performed on a Hitachi 026 CHN micro analyzer. The solvents used in the reactions were evaporated with a rotary vacuum evaporator at 40 °C.

Materials. Benzene, toluene, and tetrahydrofuran were distilled over sodium wire immediately before use. Acetone was dried over anhydrous potassium carbonate and distilled, and carbon disulfide was distilled over lime. (Trimethylsilyl)methyl azide (**1**) was prepared according to the reported method.[5] Phosphorus compounds **2**, carbonyl compounds, **4**, isocyanates **8**, and isothiocyanates **9** were commercially available and purified by distillation or recrystallization. Diphenylketene (**12**) was prepared according to the reported method.[12]

((Trimethylsilyl)methyl)iminotriphenylphosphorane (3a). A mixture of the azide **1** (1.42 g, 11 mmol) and the phosphine **2a** (2.62 g, 10 mmol) in dry benzene (10 mL) was refluxed under nitrogen for 1 h in which time nitrogen evolution ceased. The benzene was evaporated in vacuo and the residue was distilled under reduced pressure to give 3.62 g (100%) of **3a** as a colorless oil: bp 135–140 °C (3 mmHg); IR (neat) 1240, 840 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ –0.05 (s, 9, $(CH_3)_3Si$), 2.59 (d, 2, $CH_2N{=}P$, J = 23.4 Hz), 7.5–8.0 (m, 15, ArH); HRMS, m/e 363.1540 ($C_{22}H_{26}NPSi$ requires 363.1554).

Trimethyl-*N*-((trimethylsilyl)methyl)- (**3b**) and triethyl-*N*-((trimethylsilyl)methyl)phosphorimidate (**3c**) were prepared by reactions of the azide **1** with trimethyl phosphite (**2b**) and triethyl phosphite (**2c**) under the same conditions as above, respectively.

3b: yield 84%; colorless oil; bp 85–88 °C (21 mmHg); IR (neat) 1240, 840 (Me_3Si), 1040 cm^{-1} (P–O); ^1H NMR ($CDCl_3$) δ –0.05 (s, 9, $(CH_3)_3Si$), 2.50 (d, 2, $CH_2N{=}P$, J = 21.6 Hz), 3.55 (d, 9, CH_3OP, J = 13.2 Hz); NRMS, m/e 225.0977 ($C_7H_{20}NO_3PSi$ requires 225.0949).

3c: yield 87%; colorless oil; bp 101–105 °C (21 mmHg); IR (neat) 1240, 840 (Me_3Si), 1030 cm^{-1} (P–O); ^1H NMR ($CDCl_3$) δ –0.04 (s, 9, $[(CH_3)_3Si]$), 1.22 (t, 9, OCH_2CH_3, J = 8.0 Hz), 3.91 (m, 6, OCH_2CH_3); HRMS, m/e 267.1419 ($C_{10}H_{26}NO_3PSi$ requires 267.1418).

General Procedure for the One-Pot Synthesis of *N*-((Trimethylsilyl)methyl)imines (5). The typical procedure is given with an example for the synthesis of *N*-benzylidene-(trimethylsilyl)methylamine (**5a**). To a solution of triphenylphosphine (**2a**) (2.86 g, 11 mmol) in dry benzene (6 mL) was added a mixture of the azide **1** (1.42 g, 11 mmol) and benzaldehyde (**4a**) (1.06 g, 10 mmol) at room temperature. The reaction mixture was refluxed under nitrogen for 2 h. The solvent was evaporated in vacuo and the residue was triturated with hexane (50 mL). The colorless solid precipitated was removed by filtration, and the

(12) Taylor, E. C.; McKillop, A.; Hawks, G. H. *Org. Synth.* **1972**, *52*, 36.

Table II. NMR Spectral Data and E/Z Ratios of N-((Trimethylsilyl)methyl)imines 5

	^{1}H NMR, ppm [Hz][a]				^{13}C NMR, ppm[a]						
	E form		Z form		E form			Z form			
	CH_2	CH=N	CH_2	CH=N	$(CH_3)_3Si$	CH_2	CH=N	$(CH_3)_3Si$	CH_2	CH=N	E/Z
5a	3.36 (d)	8.06 (t, J = 1.5)			−2.64	54.54	157.87				100/0
5b	3.36 (d)	8.01 (t, J = 1.2)	3.45 (d)	8.13 (t, J = 2.0)	−2.70	54.54	156.28	2.52	*b*	*b*	90/10
5c	3.28 (d)	7.94 (t, J = 1.5)	3.36 (d)	8.01 (t, J = 2.0)	−2.64	54.13	157.17	*b*	47.85	161.45	80/20
5d	3.34 (d)	7.88 (t, J = 1.5)	3.43 (d)	7.99 (t, J = 1.8)	−2.64	54.84	146.95	1.94	48.14	150.94	70/30
5e	3.45 (d)	8.19 (t, J = 1.5)			−2.65	54.83	149.36				100/0
5f	3.14 (d)	7.36 (t, J = 1.5)			−2.76	53.19	168.96				100/0
5g	3.12 (br)	7.46 (m)			−2.70	53.72	162.15				100/0
5h	3.26 (d)	7.81 (m, J = 1.5)	3.36 (d)	7.81 (m, J = 2.0)	−2.64	54.89	159.98	1.64	48.08	*b*	75/25
5i	3.16 (br)	7.62 (m)	3.26 (br)	7.62 (m)	−2.70	57.07	160.16	1.94	*b*	163.92	70/30
5j			3.09 (CH_2, s)		−2.23 ($(CH_3)_3Si$), 44.91 (CH_2), 162.75 (C=N)						
5k			3.16 (CH_2 s)		−2.29 ($(CH_3)_3Si$), 43.74 (CH_2), 168.50 (C=N)						

filtrate was concentrated in vacuo. The residue was distilled under reduced pressure to give 1.69 g (89%) of the imine **5a** as a colorless oil.

Similar reactions of **1** with **2a** in the presence of other carbonyl compounds **4b–k** gave the corresponding imines **5b–k**. The reaction conditions, yields, boiling points, and NMR spectral data of **5** are given in Tables I and II, respectively.

5a: IR (neat) 1630 (C=N), 1250, 840 cm^{-1} (Me_3Si); HRMS, m/e 191.1207 ($C_{11}H_{17}NSi$ requires 191.1129). **5b**: IR (neat) 1630 (C=N), 1250, 850 cm^{-1} (Me_3Si); MS, m/e 225, 227 (M^+). Anal. Calcd for $C_{11}H_{16}NClSi$: C, 58.51; H, 7.14; N, 6.20. Found: C, 58.33; H, 7.18; N, 6.32. **5c**: IR (neat) 1630 (C=N), 1250, 850 cm^{-1} (Me_3Si); HRMS, m/e 221.1203 ($C_{12}H_{19}NOSi$ requires 221.1235). **5d**: IR (neat) 1630 (C=N), 1240, 840 cm^{-1} (Me_3Si); HRMS, m/e 181.0876 ($C_9H_{15}NOSi$ requires 181.0922). **5e**: IR (neat) 1630 (C=N), 1250, 850 cm^{-1} (Me_3Si); MS, m/e 192 (M^+). Anal. Calcd for $C_{10}H_{16}N_2Si$: C, 62.45; N, 8.38; N, 14.65. Found: C, 62.57; H, 8.28; N, 14.75. **5f**: IR (neat) 1650 (C=N), 1240, 840 cm^{-1} (Me_3Si); HRMS, m/e 171.1413 ($C_9H_{21}NSi$ requires 171.1442). **5g**: IR (neat) 1650 (C=N), 1240, 840 cm^{-1} (Me_3Si); HRMS, m/e 157.1252 ($C_8H_{19}NSi$ requires 157.1286). **5h**: IR (neat) 1630 (C=N), 1240, 840 cm^{-1} (Me_3Si); HRMS, m/e 217.1271 ($C_{13}H_{19}NSi$ requires 217.1286). **5i**: IR (neat) 1640 (C=N), 1240, 850 cm^{-1} (Me_3Si); MS, m/e 155 (M^+). Anal. Calcd for $C_8H_{17}NSi$: C, 61.87; H, 11.03; N, 9.02. Found: C, 61.57; H, 11.07; N, 9.01. **5j**: IR (neat) 1650 (C=N), 1240, 850 cm^{-1} (Me_3Si); HRMS, m/e 143.1128 ($C_8H_{15}NSi$ requires 143.1129). **5k**: IR (neat) 1640 (C=N), 1240, 850 cm^{-1} (Me_3Si); MS, m/e 183 (M^+). Anal. Calcd for $C_{10}H_{21}NSi$: C, 65.42; H, 11.54; N, 7.64. Found: C, 65.42; H, 11.44; N, 7.55.

(Trimethylsilyl)methyl Isocyanate (6). A mixture of the azide **1** (1.29 g, 10 mmol) and phosphine **2a** (2.62 g, 10 mmol) in dry THF (10 mL) was refluxed for 30 min. To the above solution under cooling was added finely crushed dry ice to cause gentle evolution of carbon dioxide gas over a period of 20 min. The solvent was evaporated in vacuo, and the residue was extracted with petroleum ether (bp 60–85 °C). After the extract was concentrated in vacuo, the residue was distilled under reduced pressure to give 0.88 g (68%) of **6** as a colorless oil: bp 51–53 °C (36 mmHg) (lit.[6a] bp 135–135.5 °C); IR (neat) 2280 (N=C=O), 1250, 840 cm^{-1} (Me_3Si); ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9, n$CH_3)_3Si$), 2.68 (s, 2, CH_2); MS, m/e 114 (M^+ − Me), 101 (M^+ − CO), 73 (Me_3Si^+, base peak).

(Trimethylsilyl)methyl Isothiocyanate (7). A mixture of the azide **1** (0.52 g, 4 mmol) and phosphine **2a** (1.05 g, 4 mmol) in dry carbon disulfide (4 mL) was stirred at room temperature for 2 h. The precipitated solid was removed by filtration and the filtrate was concentrated to leave a residue that was extracted with hexane. The extract was concentrated in vacuo and distilled under reduced pressure to give 0.55 g (94%) of **7** as a colorless oil: bp 74–79 °C (24 mmHg) (lit.[4] bp 46 °C (3 mmHg)); IR (neat) 2170, 2090 (N=C=S), 1250, 850 cm^{-1} (Me_3Si); ^{1},h NMR ($CDCl_3$) δ 0.18 (s, 9, $(CH_3)_3Si$), 2.95 (s, 2, CH_2); MS, m/e 145 (M^+).

((Trimethylsilyl)methyl)carbodiimides (10). (i) From Isocyanates 8. To a solution of iminophosphorane **3a**, which was prepared from azide **1** (1.29 g, 10 mmol) and phosphine **2a** (2.62 g, 10 mmol) in dry benzene (10 mL), was added phenyl isocyanate (**8a**) (1.19 g, 10 mmol) at room temperature. After the reaction mixture was refluxed for 1 h, the solvent was evaporated in vacuo to leave a residue that was extracted with hexane (50 mL). The extract was concentrated in vacuo, and bulb-to-bulb distillation of the residue gave 1.61 g (79%) of *N*-phenyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10a**), bp 130 °C (bath) (0.4 mmHg), as a colorless oil (the ^{1}H NMR spectrum indicated that the hexane extract contained the two carbodiimides **10a** and **11** in about a 5:1 ratio).

10a: bp 88–91 °C (0.8 mmHg); IR (neat) 2130 (N=C=N), 1250, 850 cm^{-1} (Me_3Si); ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9, $(CH_3)_3Si$), 2.81 (s, 2, CH_2), 6.9–7.3 (m, 5, ArH); ^{13}C NMR ($CDCl_3$) δ −2.94 (q, CH_3Si), 36.40 (t, CH_2), 134.10, 141.55 (each s); MS, m/e 204 (M^+). Anal. Calcd for $C_{11}H_{16}N_2Si$: C, 64.66; H, 7.89; N, 13.71. Found: C, 64.39; H, 7.92; N, 13.73.

The reaction using cyclohexyl isocyanate (**8b**) (1.41 g, 10 mmol) by the same procedure as above gave 1.67 g (79%) of *N*-cyclohexyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10b**) as a colorless oil: bp 72–74 °C (0.4 mmHg); IR (neat) 2120 (N=C=N), 1250, 850 cm^{-1} (Me_3Si); ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 9, $(CH_3)_3Si$), 1.1–2.0

(m, 10, cyclohexyl CH_2), 2.65 (s, 2, CH_2), 3.18 (m, 1, CH); MS, m/e 210 (M^+). Anal. Calcd for $C_{11}H_{22}N_2Si$: C, 62.80; H, 10.54; N, 13.31. Found: C, 62.62; H, 10.55; N, 13.24.

(ii) From Isothiocyanates 9. A solution of iminophosphorane **3a**, which was prepared from azide 1 (1.29 g, 10 mmol) and phosphine **2a** (2.62 g, 10 mmol) in dry benzene (10 mL), was refluxed with ethyl isothiocyanate (**9c**) (0.87 g, 10 mmol) for 1 h. The solvent was evaporated in vacuo, and the residue was extracted with hexane (50 mL). The extract was concentrated in vacuo, and bulb-to-bulb distillation of the residue gave 1.26 g (81%) of *N*-ethyl-*N'*-((trimethylsilyl)methyl)carbodiimide (**10c**), bp 120 °C (bath) (34 mmHg), as a colorless oil: bp 78–81 °C (26 mmHg); IR (neat) 2120 (N=C=N), 1250, 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.10 (s, 9, $(CH_3)_3Si$), 1.19 (t, 3, CH_2CH_3), 2.64 (s, 2, CH_2), 3.18 (q, 2, CH_2CH_3); MS, m/e 156 (M^+). Anal. Calcd for $C_7H_{16}N_2Si$: C, 53.79; H, 10.32; N, 17.92. Found: C, 53.77; H, 10.28; N, 17.80.

The reaction with **9a** or **9b** under the same conditions gave the carbodiimide **10a** (1.92 g, 94%) or **10b** (1.98 g, 94%), respectively.

***N,N'*-Bis((trimethylsilyl)methyl)carbodiimide (11).** A solution of iminophosphorane **3a**, which was prepared from azide **1** (1.29 g, 10 mmol) and phosphine **2a** (2.62 g, 10 mmol) in dry benzene (10 mL), was refluxed with phenyl isocyanate (**8a**) (0.59 g, 5 mmol) for 2 h. The solvent was evaporated in vacuo, and the residue was extracted with hexane (10 mL × 2). The extract was concentrated in vacuo, and the residue was distilled under reduced pressure to give 1.04 g (97%) of **11**, bp 77–80 °C (23 mmHg), as a colorless oil: IR (neat) 2120 (N=C=N), 1250, 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.09 (s, 18, $(CH_3)_3Si$), 2.60 (s, 4, CH_2); MS, m/e 214 (M^+). Anal. Calcd for $C_9H_{22}N_2Si_2$: C, 50.41; H, 10.34; N, 13.06. Found: C, 50.65; H, 10.23; N, 13.13.

The reaction of iminophosphorane **3a** with 1 equiv of carbodiimide **10a** in refluxing benzene for 1 h afforded **11** in a quantitative yield.

Diphenylketene *N*-((Trimethylsilyl)methyl)imine (13). A solution of iminophosphorane **3a**, which was prepared from azide **1** (1.29 g, 10 mmol) and phosphine **2a** (2.62 g, 10 mmol) in dry benzene (10 mL), was refluxed witthdiphenylketene (**12**) (1.94 g, 10 mmol) for 1 h. The solvent was evaporated in vacuo, and the residue was extracted with hexane (50 mL). The extract was concentrated in vacuo, and the residue was distilled under reduced pressure to give 2.60 g (93%) of **13**, bp 132–136 °C (1.0 mmHg), as a colorless oil: IR (neat) 2000 (N=C=C), 1250, 850 cm^{-1} (Me_3Si); ^1H NMR ($CDCl_3$) δ 0.06 (s, 9, $(CH_3)_3Si$), 3.16 (s, 2, CH_2e, 7.1–7.4 (m, 10, ArH); ^{13}C NMR ($CDCl_3$) δ −2.70 (q, CH_3), 44.27 (t, CH_2), 73.86 (s, N=C=*C*), 183.29 (s, N=*C*=C); MS, m/e 279 (M^+). Anal. Calcd for $C_{18}H_{21}NSi$: C, 77.36; H, 7.57; N, 5.06. Found: C, 77.21; H, 7.49; N, 4.80.

Registry No. 1, 87576-94-1; **2a**, 603-35-0; **2b**, 121-45-9; **2c**, 122-52-1; **3a**, 90606-07-8; **3b**, 90606-08-9; **3c**, 90606-09-0; **4a**, 100-52-7; **4b**, 104-88-1; **4c**, 123-11-5; **4d**, 98-01-1; **4e**, 1121-60-4; **4f**, 630-19-3; **4g**, 123-72-8; **4h**, 14371-10-9; **4i**, 123-73-9; **4j**, 67-64-1; **4k**, 108-94-1; **5a**, 90606-10-3; (*E*)-**5b**, 90606-11-4; (*Z*)-**5b**, 90606-12-5; (*E*)-**5c**, 90606-13-6; (*Z*)-**5c**, 90606-14-7; (*E*)-**5d**, 90606-15-8; (*Z*)-**5d**, 90606-16-9; **5e**, 90623-29-3; **5f**, 90606-17-0; **5g**, 90606-18-1; (*E*)-**5h**, 90606-19-2; (*Z*)-**5h**, 90606-20-5; (*E*)-**5i**, 90606-21-6; (*Z*)-**5i**, 90606-22-7; **5j**, 90606-23-8; **5k**, 90606-24-9; **6**, 14283-35-3; **7**, 18293-48-6; **8a**, 103-71-9; **8b**, 3173-53-3; **9a**, 103-72-0; **9b**, 1122-82-3; **9c**, 542-85-8; **10a**, 90606-25-0; **10b**, 90606-26-1; **10c**, 90606-27-2; **11**, 90606-28-3; **12**, 525-06-4; **13**, 90606-29-4; CO_2, 124-38-9; CS_2, 75-15-0.

Novel Synthesis of 3,5-Disubstituted Pyridines by 1,4-Cycloaddition of 1-Aza-1,3-butadienes with Enamines

Mitsuo Komatsu, Shigeki Takamatsu, Masatoshi Uesaka, Shinji Yamamoto, Yoshiki Ohshiro,* and Toshio Agawa

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamada-oka 2-1, Suita, Osaka 565, Japan

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A new method for the synthesis of 3,5-disubstituted pyridines is described. Reactions of the N-substituted methanimines **1** with the β-substituted enamines **2** give 1-aza-1,3-butadienes **3a–i** and/or symmetrically 3,5-disubstituted pyridines **4a–c,e–h** in moderate to good yields. At reaction temperatures of 150 °C the azadienes **3** are the predominant products, and the reaction provides a good route to 1-azadienes with no substituent at the 4-position. At reaction temperatures of 200 °C, and particularly using *N-tert*-butylmethanimine **1a** and *p*-toluenesulfonic acid catalyst, the principal products are symmetrically 3,5-disubstituted pyridines. The cycloaddition was shown to proceed via the azabutadiene intermediate **3**. Reactions of **3** with the enamines **2** lead to unsymmetrically 3,5-disubstituted pyridines. The mechanisms of these cycloadditions are discussed.

The pyridine ring system is often found in alkaloids and in compounds used in pharmacy and agriculture.[1] In a preliminary report,[2] we described a new preparation of symmetrically 3,5-disubstituted pyridines from *N-tert*-butylmethanimine and enamines by cycloaddition of a 1-aza-1,3-butadiene with an enamine. Although 3,5-disubstituted pyridines have not been extensively investigated,[3] 3(or 5)-alkyl- or 3,5-dialkylpyridine derivatives are useful precursors of pyridine mono- or dicarboxylic acids,[3] which are directly related to nicotinoids or to pyridine-containing macrocycles.[4]

There are several reports on reactions of imines with enamines,[5] but formation of a pyridine ring has not been observed. We have reported on the isolation of 1-azabutadienes,[2] and recently Nomura et al. reported formation of 1,2,4-triaryl-substituted 1-azabutadienes from aryl-substituted imines and enamines.[5b]

We here report on further investigations of the addition of *N*-substituted methanimines to enamines for the syn-

(1) Glasby, J. S. "Encyclopedia of the Alkaloids"; Plenum Press: New York, 1975. Weissberger, A. "Pyridine and Its Derivatives"; Wiley-Interscience: New York, 1960. Abramovitch, R. A. "Pyridine and Its Derivatives"; Wiley-Interscience: New York, 1975; Supplement.

(2) Komatsu, M.; Ohgishi, H.; Takamatsu, S.; Ohshiro, Y.; Agawa, T. *Angew. Chem.* **1982**, *94*, 214. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 213. *Angew. Chem. Suppl.* **1982**, 483.

(3) Dietrich, D.; Reiff, H.; Ziemann, H.; Braden, R. *Liebigs Ann. Chem.* **1973**, 111 and references cited therein.

(4) See for example: Deuchert, K.; Hünig, S. In "New Trends in Heterocyclic Chemistry"; Mitra, R. B., et al., Eds.; Elsevier: Amsterdam, 1979; pp 202–215.

(5) (a) Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Tetrahedron Lett.* **1969**, 3549. Nomura, Y.; Tomoda, S.; Takeuchi, Y. *Chem. Lett.* **1972**, 79. Nomura, Y.; Kimura, M.; Takeuchi, Y.; Tomoda, S. *Ibid.* **1978**, 427. (b) Nomura, Y.; Kimura, M.; Shibata, T.; Takeuchi, Y.; Tomoda, S. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3343.

0022-3263/84/1949-2691$01.50/0