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Synthesis and molecular properties of formic hydrazides

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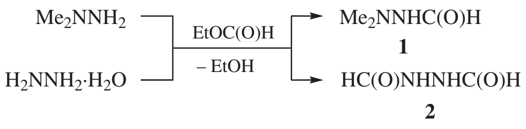
The existence of 1,3-silatropic transformation in *N′,N′*-dimethyl-*N*-(trimethylsilyl)formic hydrazide was discovered. In the crystal, its molecules form chains due to bifurcated hydrogen bonds.

Formamides are an important class of nitrogen-containing organic compounds used as anticancer chematherapeutic agents,[1] precursors of fungicides and herbicides[2] and starting materials in the preparation of linear and heterocyclic compounds.[3–5] They are obtained mostly by N-formylation of amines[1–4] or their organosilicon derivatives.[5–7]

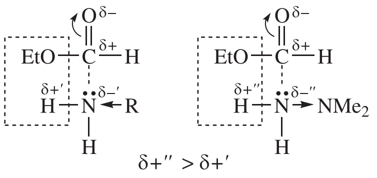
In the case of highly nucleophilic amines, formylation with alkyl formates proceeds cleanly under heating and completes after alcohol release stops.[8–10] In this manner *N*-(4-methoxyphenyl)formamide was herein obtained.[†] The process temperature can be reduced to ambient one with significant raising products yields on using 'HEV[13]' zeolite as a catalyst.

On moving to less nucleophilic hydrazines or their hydrates, the process nature is changed and formylhydrazides can be obtained in quantitative yields only at low temperature (~0 °C, Scheme 1).[‡]



Scheme 1

Such an effect can be explained by the increase in hydrogen acidity at nitrogen in hydrazines due to the influence of a neighboring electronegative substituent resulting in easier deprotonation in comparison with high-basic amines (Scheme 2).



Scheme 2

In the ^{1}H NMR spectrum of compound **2**, formyl protons resonate as two singlets, and dimethylamino protons also resonate as two singlets. This indicates the hindrance in rotation of N=C(O) bond in the molecule **1**.

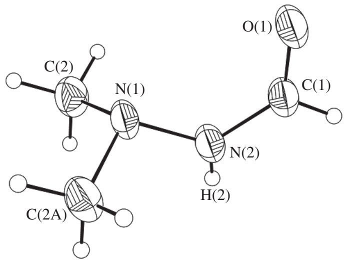


Figure 1 Molecular structure of *N′,N′*-dimethylformic hydrazide **1**. Selected bond lengths (Å) and angles (°): O(1)–C(1) 1.231(3), N(1)–N(2) 1.420(3), N(1)–C(2) 1.4691(17), C(1)–N(2) 1.329(3), N(2)–H(2) 0.92; N(2)–N(1)–C(2) 109.33(13), C(2)–N(1)–C(2A) 111.84(18), O(1)–C(1)–N(2) 126.6(2), C(1)–N(2)–N(1) 120.0(2), C(2)–N(1)–N(2)–C(1) 118.63(13). The C(2A) atom was obtained from the base one by means of symmetrical transformation of $-x + 1, y, z$.

[†] IR spectra were recorded on a Specord 75 IR instrument in Nujol. ^{1}H NMR spectra were recorded on Bruker WP-300 (300 MHz) and Bruker DRX500 (500 MHz) spectrometers in C_6D_6 or $CDCl_3$.

N-*(4-Methoxyphenyl)formamide*. A mixture of 4-methoxyaniline (10 g, 0.0812 mol) and ethyl formate (6.02 g, 0.0812 mol) was heated at 100 °C for 1 h until evolution of ethanol ceased. The crystals formed were filtered giving 11.04 g (90%) of the product, mp 76–78 °C. IR (KBr, ν/cm^{-1}): 3240 (N–H), 3190 (C–H), 1670 (C=O). ^{1}H NMR (300 MHz, C_6D_6) δ: 3.25 (s, 3H, OMe), 6.22 (br. s, 1H, NH), 6.71 (d, 2H, CH), 7.43 (d, 2H, CH), 7.82 (1H, CH). Found (%): C, 63.55; H, 5.95; N 9.25. Calc. for $C_7H_9NO_2$ (%): C, 63.5; H, 5.95; N, 9.26.

[‡] N′,N′-*Dimethylformic hydrazide* **1**. A mixture of *N′,N′*-dimethylhydrazine (21.53 g, 0.36 mol) and ethyl formate (26.54 g, 0.36 mol) was kept at ~0 °C for 12 h. The crystals formed were filtered to give 31.06 g (99%) of compound **1**, mp 59–60 °C. IR (KBr, ν/cm^{-1}): 3320 (N–H), 3160 (C–H), 1640 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.45 and 2.48 (s, 3H, CMe), 6.51 (br. s, 1H, NCH), 8.17 and 8.19 (s, 1H, CH). Found (%): C, 40.95; H, 9.19; N, 31.83. Calc. for $C_3H_8N_2O$ (%): C, 40.90; H, 9.15; N, 31.79.

N,N′-*Diformylhydrazine* **2**. A mixture of hydrazine monohydrate (10.5 g, 0.21 mol) and ethyl formate (31.2 g, 0.42 mol) was kept at 0 °C for 48 h. The crystals formed were filtered to afford 36.54 g (99%) of compound **2**, mp 155–156 °C. IR (KBr, ν/cm^{-1}): 3300 (N–H), 3140 (C–H), 1620 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.91 and 8.14 (d, 1H, CH), 9.95 (br. s, 2H, NH). Found (%): C, 27.32; H, 4.60; N, 31.87. Calc. for $C_2H_4N_2O_2$ (%): C, 27.28; H, 4.58; N, 31.81.

N′,N′-*Dimethyl*-N-*(trimethylsilyl)formic hydrazide* **3**. A mixture of compound **1** (10.04 g, 0.114 mol), chlorotrimethylsilane (12.38 g, 0.114 mol), triethylamine (16.19 g, 0.160 mol) and 100 ml of diethyl ether was stirred at 35 °C for 10 h. Then, triethylamine hydrochloride was filtered off. The filtrate was distilled to give 15.71 g (86%) of product **3**, bp 143–144 °C, n_D^{20} 1.4305. IR (KBr, ν/cm^{-1}): 3160 (C–H), 1650 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.3 (s, 9H, SiMe), 2.4 (s, 6H, NMe), 7.62 [s, 1H, C(O)H]. Found (%): C, 44.95; H, 10.03; N, 17.42; Si, 17.56. Calc. for $C_6H_{16}N_2OSi$ (%): C, 44.96; H, 10.01; N, 17.48; Si, 17.52.

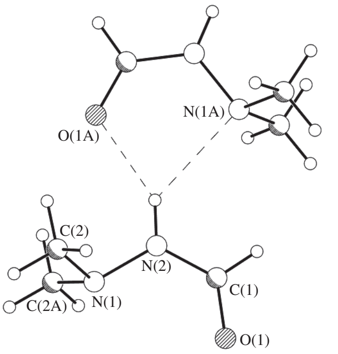
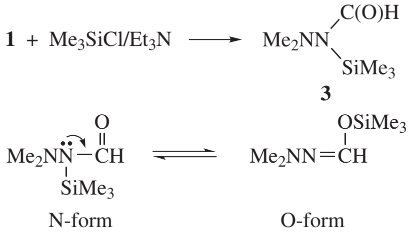


Figure 2 Association of *N′*,*N′*-dimethylformic hydrazide **1** molecules.

X-ray structure analysis data also confirm the presence of $\mathrm{C\overset{\curvearrowleft}{-}\ddot{N}}$ effect (Figure 1). The C(1)–N(2) bond length is 1.329 Å being shortened in comparison with ordinary C–N bond length of 1.472 Å.

In the crystal (Figure 2)[§] molecules of compound **1** form chains due to bifurcated hydrogen bonds N(2)–H(2)···O(1) (–*x* + 1, –*y* + 1, *z* – 1/2) [H(2)···O(1) 2.06 Å, N(2)···O(2) 2.877(3) Å, N(2)–H(2)–O(1) 148°] and N(2)–H(2)···N(1) (–*x* + 1, –*y* + 1, *z* – 1/2) [H(2)···N(2) 2.47 Å, N(2)···N(1) 3.200(2) Å, N(2)–H(2)–N(1) 137°].

Formic hydrazide **1** is readily silylated giving new *N′*,*N′*-dimethyl-*N*-(trimethylsilyl)formic hydrazide **3** (Scheme 3).[‡] As for other trimethylsilyl derivatives of carboxamides, 1,3-silatropic migration is typical of compound **3**. This was confirmed by IR, ^{1}H, ^{13}C, ^{15}N and ^{29}Si NMR spectra.



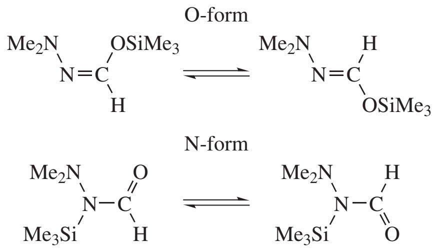
Scheme 3

Due to partial $\mathrm{C\overset{\curvearrowleft}{-}\ddot{N}}$ bond order (in N-isomer) and full N=C bond order (in O-isomer), inequivalence of nuclei shielding (^{1}H, ^{13}C, ^{15}N, ^{29}Si) in *cis*- and *trans*-positions occurs (Table 1). ^{29}Si NMR spectrum contains four signals in pairs in two specific regions: 22.70 and 20.83 ppm (OSiMe$_3$) in a downfield region and 10.76 and 7.70 ppm (NSiMe$_3$) in an upfield region. Signals of NSiMe$_3$ groups are significantly broadened due to ^{15}N and ^{29}Si spin–spin interaction. The presence of two ^{29}Si signals for O- and N-forms is owing to the possibility of *cis*/*trans* isomerism in respect of N=C bond in O-form and in respect of $\mathrm{N\overset{\cdots}{-}C}$ bond of N–C=O grouping in N-form. In total, the equilibrium mixture consists of four isomers (Scheme 4).

Table 1 ^{1}H, ^{13}C and ^{15}N NMR spectra of *N′*,*N′*-dimethyl-*N*-(trimethylsilyl)-formic hydrazide **3** (in CDCl$_3$).

Isomer	$\delta_{^1\mathrm{H}}$/ppm		$\delta_{^{13}\mathrm{C}}$/ppm			$\delta_{^{15}\mathrm{N}}$/ppm	
	CH	NMe$_2$	CH	NMe$_2$	SiMe$_3$	NCH	NMe$_2$
cis-O-form	6.90	1.88	149.12	46.01	–1.20	–70	–289
trans-O-form	5.99	1.95	138.27	45.60	–1.47	–83	–299
cis-N-form[a]	7.57	2.24	161.48	43.07	–2.42	–208	–309

[a] Due to low (~2%) *trans*-N-form content its signals were missed.



Scheme 4

In conclusion, we have found that the conditions for formylation of amines and hydrazines used depend on nucleophilicity of the nitrogen-containing organic compounds. The possibility of 1,3-silatropic transformation has been demonstrated not only for silicone acid amides but also for formic hydrazide. X-ray structure analysis showed the presence of bifurcated hydrogen bonds in the crystal of *N′*,*N′*-dimethylformic hydrazide.

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[§] *Crystal data*. Orthorhombic crystals of **1** were obtained from ethanolic solution, composition C$_3$H$_8$N$_2$O, space group *Cmc*2$_1$, *a* = 9.5620(14), *b* = 6.7353(14) and *c* = 7.9152(13) Å, *V* = 509.76(15) Å^3, *Z* = 4, *M* = 88.11, d_calc = 1.148 g cm^{-3}, μ(MoKα) = 0.87 cm^{-1}, *F*(000) = 192. The intensities of 2747 reflections were measured on a Smart APEX II diffractometer at 100 K [λ(MoKα) = 0.71073 Å, ω-scanning, $2\theta_\mathrm{max}$ = 30.0°]; 416 independent reflections (R_int = 0.0565) were used for solving and refining the structure. The structure was solved by direct method and refined by full-matrix technique against F^2 in the anisotropic approximation. The positions of hydrogen atoms were calculated geometrically and refined in rigid body approximation. Final *R* factors: R_1 = 0.0374 [386 reflections with $I > 2\sigma(I)$], wR_2 = 0.1079 (all reflections), GOF = 0.998. All calculations were carried out with SHELXTL ver. 5.10 program complex.[11]

CCDC 1049145 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.