

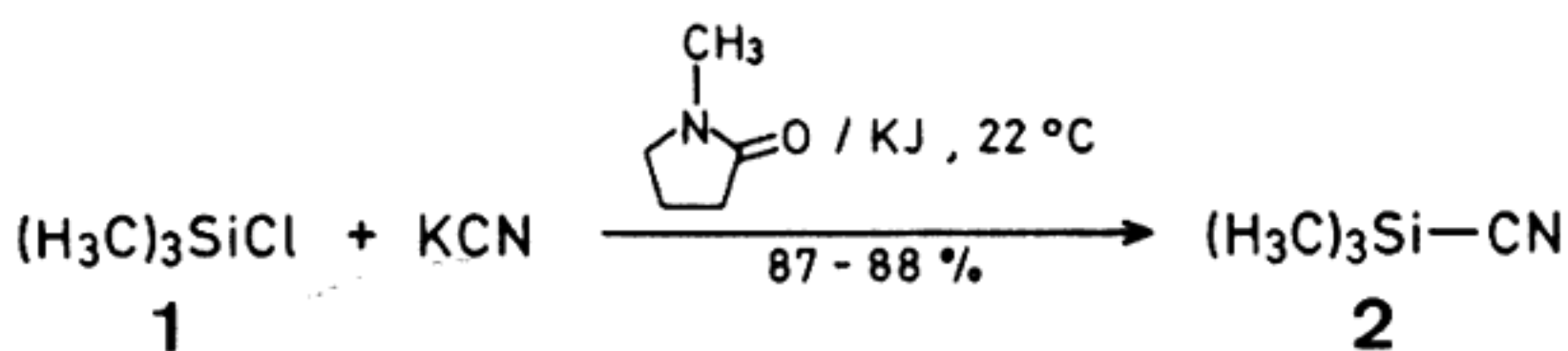
An Improved Synthesis of Cyanotrimethylsilane

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Synthesis 330 (1982)

Cyanotrimethylsilane (**2**) is an excellent reagent for a number of useful reactions such as the conversion of aldehydes and ketones into silylated cyanohydrins, which in turn are versatile synthetic intermediates¹. The currently best syntheses of **2** are the reaction of chlorotrimethylsilane (**1**) with a 22% excess of sodium cyanide in *N*-methylpyrrolidinone in the presence of a phase-transfer catalyst (30–36 h, 90–100°C; yield: 60–70%)² and the reaction of chlorotrimethylsilane (**1**) with a 250% excess of potassium cyanide in boiling *N*-methylpyrrolidinone (16 h, yield: 71%)^{3,4}.

We report here that cyanotrimethylsilane (**2**) can be prepared in 87–88% yield by the reaction of equimolecular amounts of chlorotrimethylsilane (**1**) and potassium cyanide in the presence of 10 mol% of potassium iodide and 20 mol% of *N*-methylpyrrolidinone at room temperature for 12 h. Under these conditions, conversion is complete and the product can be distilled directly from the reaction flask. The reaction proceeds equally well if sodium cyanide and sodium iodide are used, the reaction conditions being the same. A third version using potassium or sodium cyanide and potassium or sodium iodide in the absence of *N*-methylpyrrolidinone is possible, but requires considerably longer reaction times (75 h).



The catalytic effect of potassium or sodium iodide in these reactions may be rationalized by assuming the intermediate formation of iodo-trimethylsilane which is known to be a highly reactive electrophile¹.

Cyanotrimethylsilane (**2**):

Performance of the reaction under an inert gas atmosphere is not necessary but exposure of the reaction mixture or the product to air should be avoided.

Method A, in *N*-Methylpyrrolidinone as Solvent: *N*-Methylpyrrolidinone (19.8 g, 0.2 mol) is gradually added to a stirred suspension of dry potassium cyanide (finely divided and having been kept in a drying pistol at 120°C under vacuum for 24 h before use; 65.1 g, 1 mol) and potassium iodide (16.6 g, 0.1 mol) in chlorotrimethylsilane (**1**; 108.2 g, 1 mol) in a dried round-bottom flask, and stirring is continued at room temperature for 12 h, after which time the ¹H-N.M.R. spectrum of the crude product indicates complete conversion. Product **2** is distilled directly from the reaction flask; yield: 86–87.2 g (87–88%); b.p. 112–117°C (Ref.³, b.p. 114–117°C); m.p. 7–10°C; purity: >96% (G.L.C. analysis, Chromosorb SE 30, 3% silicon, 70°C). The ¹H-N.M.R. (CCl₄/TMS) spectrum shows no impurities (singlet at δ=0.1 ppm).

The above reaction proceeds completely in the same manner when sodium cyanide and sodium iodide are used; yield: 87–88%.

Method B, without Solvent: A suspension of sodium cyanide (9.8 g, 0.2 mol) and sodium iodide (3.0 g, 0.02 mol) in chlorotrimethylsilane (**1**; 21.6 g, 0.2 mol) is vigorously stirred at room temperature for 75 h. Work-up as in Method A affords **2** having the same purity as in Method A; yield: 17 g (85%).

¹ W. C. Groutas, D. Felker, *Synthesis* **1980**, 861.

² S. Hünig, G. Wehner, *Synthesis* **1979**, 522.

³ J. K. Rasmussen, S. M. Heilmann, *Synthesis* **1979**, 523.

⁴ Note added in proof: **2** can also be prepared in yields of 59–82% by the reaction of acetone cyanohydrin and lithium hydride followed by quenching the lithium cyanide with chlorotrimethylsilane; *Org. React.* **60**, 126 (1981).

A Simple, Safe, and Inexpensive Preparation of Trimethylsilyl Cyanide

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Synthesis 523 (1979)

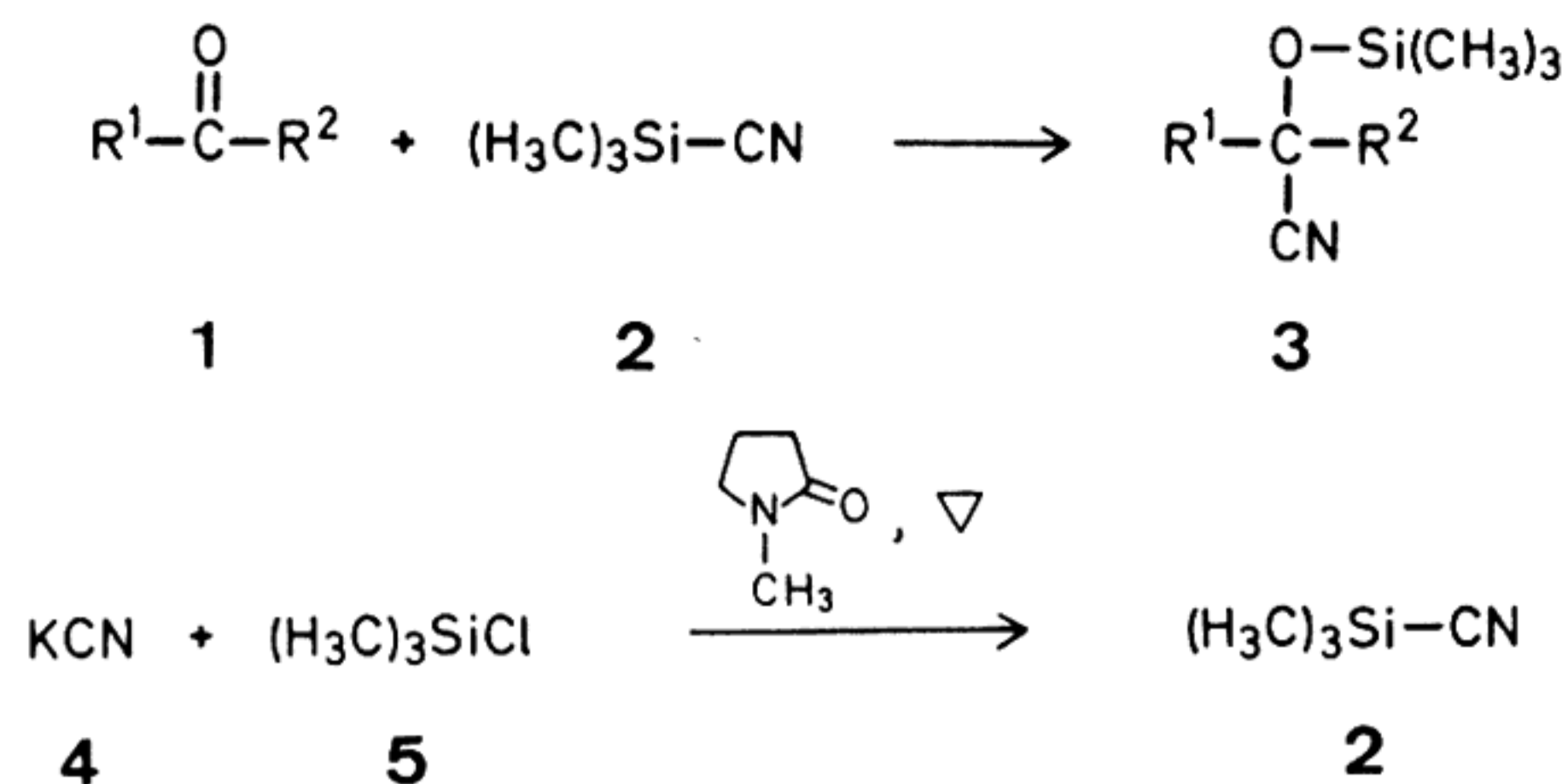
In recent years, trimethylsilyl cyanide (**2**) has been shown to be an excellent reagent for the direct conversion of aldehydes and ketones **1** into silylated cyanohydrins **3**¹⁻⁵. The excellent yields, exclusive 1,2-additions to α,β -unsaturated carbonyl compounds, and ease of adduct formation even with ketones that are normally resistant to cyanohydrin formation make this reaction one of the few truly general transformations in synthetic organic chemistry.

Silylated cyanohydrins have found considerable synthetic utility in the regioselective protection of *p*-quinones⁶, as precursors to acyl anion equivalents^{7,8,9}, as intermediates for the preparation of β -aminomethyl alcohols³, and as precursors to certain cyanohydrins themselves¹⁰. In addition, α -amino amides and α -amino acids have been prepared via addition of **2** to Schiff bases and oximes^{11,12}.

To date, numerous preparations of **2** have been described, the majority of which have basically utilized one of two approaches: (1) use of the very expensive reagent silver cyanide or (2) procedures requiring the handling of extremely toxic hydrogen cyanide¹³. Two recent, improved preparations^{14,15} are merely modifications of these two approaches and, although they offer some advantages, are still only marginal improvements.

We recently reported¹⁶ that aldehydes and ketones can be cyanosilylated by heating with a mixture of potassium cyanide and trimethylsilyl chloride in an appropriate solvent such as acetonitrile or dimethylformamide. At that time we postulated that **2** might be formed *in situ* as an intermediate in the reaction. Due to our inability to extend this *in situ* cyanosilylation procedure to the imine system¹⁷, and the general utility of **2**, we decided to investigate the possibility of preparing **2** directly from potassium cyanide and trimethylsilyl chloride.

We have now found that potassium cyanide can quite efficiently be utilized for the synthesis of **2** and, contrary to previous belief¹⁵, without the need for crown ether catalysis. Simply heating a mixture of trimethylsilyl chloride and potassium cyanide in a dipolar aprotic solvent produces **2** in good yield and purity. For convenience, *N*-methylpyrrolidinone was chosen as the solvent. The choice of a high boiling solvent (b.p. 202°) allows for easy monitoring of the reaction (one simply follows the reflux temperature as it changes from 57°, the b.p. of trimethylsilyl chloride, to that of **2**). Then **2** is readily distilled directly from the pot.



Utilizing this procedure, **2** was obtained in 71% yield; the yield should not be considered optimum since scrupulous drying of the glassware and solvent was not performed.

The simplicity of this procedure suggests its modification for the preparation of a number of other useful organosilanes such as trimethylsilyl azide, trimethylsilyl isocyanate, and trimethylsilyl iodide.

Trimethylsilyl Cyanide (**2**):

Dry potassium cyanide (65 g, 1 mol), trimethylsilyl chloride (43.4 g, 0.4 mol) and *N*-methylpyrrolidinone (100 ml) are placed in a 1000 ml flask. The contents are then stirred mechanically and heated overnight (16 h), by which time the reflux temperature had reached ~105°. A distillation head and short column (15 cm) are attached and, after collecting a small forerun containing a mixture of hexamethyldisiloxane and **2**, the pure product is collected; yield: 28.0 g (71%); b.p. 115–118° (Lit.³ b.p. 114–117°, 117–118°); n_D^{20} : 1.3897; purity by G.L.C. $\geq 98\%$.

- 1 D. A. Evans, L. K. Truesdale, G. L. Carroll, *J. Chem. Soc. Chem. Commun.* **1973**, 55.
- 2 D. A. Evans, L. K. Truesdale, *Tetrahedron Lett.* **1973**, 4929.
- 3 D. A. Evans, G. L. Carroll, L. K. Truesdale, *J. Org. Chem.* **39**, 914 (1974).
- 4 W. Lidy, W. Sundermeyer, *Chem. Ber.* **106**, 587 (1973).
- 5 H. Neef, R. Müller, *J. Prakt. Chem.* **315**, 367 (1973).
- 6 D. A. Evans, J. M. Hoffman, L. K. Truesdale, *J. Am. Chem. Soc.* **95**, 5822 (1973).
- 7 K. Deuchert, U. Hertenstein, S. Hünig, *Synthesis* **1973**, 777.
- 8 S. Hünig, G. Wehner, *Synthesis* **1975**, 180.
- 9 S. Hünig, G. Wehner, *Synthesis* **1975**, 391.
- 10 D. Boutte, A. Auroux, *French Patent* 2321484, 1977; *C. A.* **88**, 37454 (1978).
- 11 I. Ojima, S. Inaba, K. Nakatsugawa, Y. Nagai, *Chem. Lett.* **1975**, 331.
- 12 I. Ojima, S. Inaba, Y. Nagai, *Chem. Lett.* **1975**, 737.
- 13 Evans et al., reference 3, describe in detail the use of both of these procedures.
- 14 I. Ryu, S. Murai, T. Horiike, A. Shinonaga, N. Sonoda, *Synthesis* **1978**, 154.
- 15 B. Uznanski, W. J. Stec, *Synthesis* **1978**, 154.
- 16 J. K. Rasmussen, S. M. Heilmann, *Synthesis* **1978**, 219.
- 17 Aldoximes are dehydrated to nitriles in high yield under these conditions, J. K. Rasmussen, *Chem. Lett.* **1977**, 1295.

Eine einfache und ergiebige Synthese von Trimethylsilyl-cyanid

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In einer sehr allgemeinen Reaktion addiert sich Trimethylsilyl-cyanid (**2**) leicht und glatt an Aldehyde und Ketone unter Katalyse von Lewis-Säuren¹⁻⁴. Da die Carbonyl-Funktion unter milden Bedingungen regeneriert werden kann¹⁻⁵, hat **2** als Schutzgruppenreagenz, aber auch als wirksames Umpolungsreagenz zur nucleophilen Acylierung mit (hetero)aromatischen und konjugiert ungesättigten Aldehyden Bedeutung erlangt^{5,6,7}.

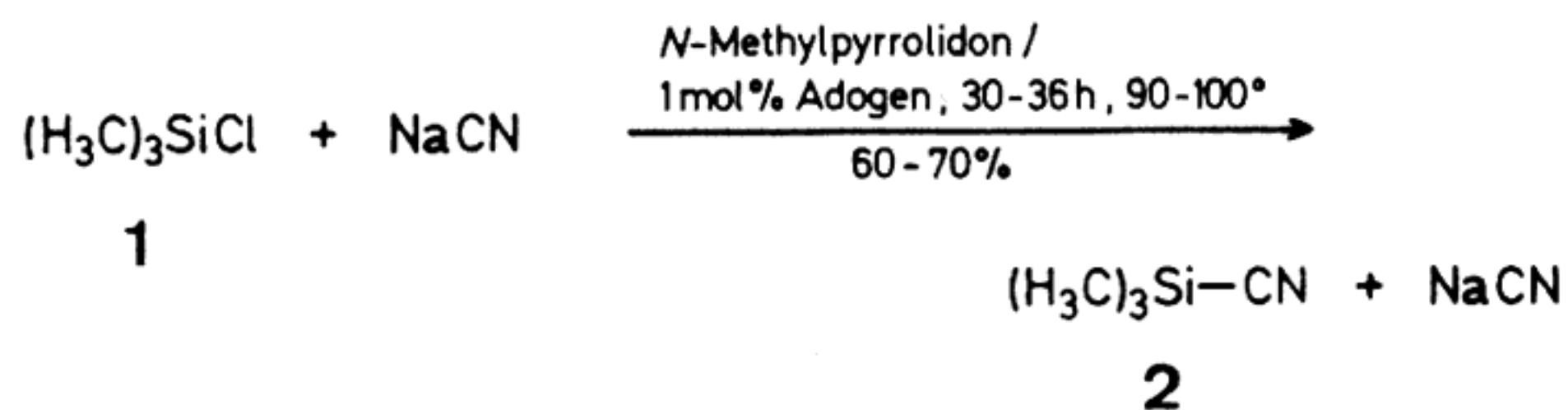
Nachdem die bisher bekannten Verfahren zur Herstellung von **2** teure (Silbercyanid⁸) oder schwierig zu handhabende (Cyanwasserstoff^{9,10,11}) Ausgangsmaterialien erfordern bzw. einen hohen apparativen Aufwand verlangen^{12,13}, stellen wir hier eine einfache Synthese für **2** im 4-6-Mol-Maßstab vor, die sich der billigen Reagentien Chlorotrimethylsilan (**1**) und Natriumcyanid (in aprotischen Lösungsmitteln besser löslich als Kaliumcyanid¹⁴) bedient. Als Solvens eignet sich das billige *N*-Methylpyrrolidon; Dimethylsulfoxid und Dimethylformamid¹⁵ sind gegen Chlorotrimethylsilan bzw. **2** nicht inert. Der Zusatz des Phasentransfer-Katalysators Adogen 464¹⁶ ist entscheidend, da die Ausbeute an **2** sonst nur 20-30% beträgt. Wegen seines hohen Siedepunktes bietet *N*-Methylpyrrolidon vor allem bei größeren Ansätzen den zusätzlichen Vorteil, daß sich **2** aus dem Reaktionsgemisch abdestillieren läßt, so daß dieses anschließend verworfen werden kann.

Trimethylsilyl-cyanid (**2**):

N-Methylpyrrolidon wird durch Destillation über Calciumhydrid getrocknet. Natriumcyanid wird 24 h bei 120° getrocknet; mit gemahlenem Natriumcyanid wird eine erhöhte Reaktionsgeschwindigkeit erzielt. Die Reaktion wird in einem Dreihalskolben mit Rührer und Rückflußkühler durchgeführt. Die Reaktionsgefäße werden ausgeheizt und mit Stickstoff durchspült.

Zu einer Suspension von Natriumcyanid (300 g, 6.12 mol) in *N*-Methylpyrrolidon (500 ml) gibt man unter Rühren Adogen 464[®] (24 g, 60 mmol) und Chlorotrimethylsilan (**1**; 540 g, 5.00 mmol) und erhitzt das Gemisch so lange auf 90-100°, bis das ¹H-N.M.R.-Spektrum einer Probe weitgehenden Umsatz (nach ~30-36 h) anzeigt (Chlorotrimethylsilan: $\delta = 0.3$ ppm; Trimethylsilyl-cyanid: $\delta = 0.1$ ppm). Die flüchtigen Bestandteile werden anschließend im Wasserstrahl-Vakuum über eine Claisen-Brücke bis zu einer Badtemperatur von 70° abdestilliert, wobei die Vorlage mit Methanol/Trockeneis gekühlt wird. Das Destillat wird über eine 40-cm-Ringspalt-Kolonnen fraktioniert; Ausbeute an **2**: 297-347 g (60-70%); Kp: 117-118° (Lit.¹¹, Kp: 117°).

Das Produkt bleibt bei diesem Reinheitsgrad unter Luftabschluß im Dunkeln monatelang farblos. Im N.M.R.-Spektrum sind keine Verunreinigungen zu erkennen.



¹ W. Lidy, W. Sundermeyer, *Chem. Ber.* **106**, 687 (1973).

² H. Neef, H. Müller, *J. prakt. Chem.* **315**, 367 (1973).

³ D. A. Evans, L. K. Truesdale, *Tetrahedron Lett.* **1973**, 4929.

⁴ D. A. Evans, J. M. Hoffmann, L. K. Truesdale, *J. Am. Chem. Soc.* **95**, 5822 (1973).

⁵ K. Deuchert, U. Hertenstein, S. Hünig, *Synthesis* **1973**, 777.
S. Hünig, G. Wehner, *Synthesis* **1975**, 391.

⁶ S. Hünig, G. Wehner, *Synthesis* **1975**, 180.

⁷ U. Hertenstein, S. Hünig, M. Öller, *Synthesis* **1976**, 416.

⁸ J. J. McBride, H. C. Beachell, *J. Am. Chem. Soc.* **74**, 5247 (1952).

C. Eaborn, *J. Chem. Soc.* **1950**, 3077.

E. C. Evers, W. O. Freitag, J. N. Kneith, *J. Am. Chem. Soc.* **81**, 4493 (1959).

⁹ D. A. Evans, *J. Org. Chem.* **39**, 914 (1974).

¹⁰ B. Uznanski, W. J. Stec, *Synthesis* **1978**, 154.

¹¹ T. A. Bither, W. H. Knoth, R. v. Lindsey, W. H. Sharky, *J. Am. Chem. Soc.* **80**, 4151 (1958).

¹² W. Sundermeyer, *Z. Anorg. Allg. Chem.* **313**, 290 (1962).

Beim Durchleiten von Chlorotrimethylsilan durch die KCN enthaltende Salzsäuremelze von LiCl/KCl entsteht **2** sofort rein in 80% Ausbeute.

¹³ Weitere Verfahren zur Synthese von **1**:

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¹⁴ A. J. Parker, *Quart. Rev. Chem. Soc.* **16**, 163 (1962).

¹⁵ Dimethylformamid reagiert mit Chlorotrimethylsilan bei verlängerten Reaktionszeiten zu Hexamethyldisiloxan: E. G. Rochow, K. Gingold, *J. Am. Chem. Soc.* **76**, 4852 (1954).

¹⁶ Verwendung von Adogen 464[®] für Phasentransfer-Katalyse fest→flüssig: H. Jonczyk, M. Ludwikow, M. Mąkosza, *Angew. Chem.* **90**, 58 (1978); *Angew. Chem. Int. Ed. Engl.* **17**, 62 (1978).