Tetrahedron Letters No. 20, pp 2057 - 2060, 1972. Pergamon Press. Printed in Great Britain.

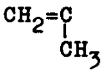
REACTION OF N-TRIMETHYL SILYL AMIDES WITH ACID CHLORIDES.
AN EASY SYNTHETIC ROUTE TO NITRILES.

Manfred L. Hallensleben
Institute of Macromolecular Chemistry, University of Freiburg,
78 Freiburg i.Br., Stefan-Meier-Str. 31, Germany

(Received in UK 5 April 1972; accepted for publication 12 April 1972)

The reaction of N-trimethyl silyl amides (1,2) with either aliphatic or aromatic acid chlorides (3) to yield nitriles (6,7) opens a new synthetic route for the conversion of amides via N-trimethylsilylation [1,2] into nitriles. Since the silylation reaction of amides using trimethyl chlorosilane and triethyl amine under benzene refluxing conditions [1] proceeds in almost 90 % yield, the reactive N-silylated amide intermediate (1,2) in this reaction is easy to obtain and to purify by distillation [2].

$$\underset{(1,2)}{R\text{-}\left(\text{CO-NH-Si}(CH_3)_3\right)_n} + \underset{(3)}{n\ \text{Cl-CO-R'}} \xrightarrow[\substack{-\ n\ \text{Cl-Si}(CH_3)_3\\ (4)}]{} \underset{(6,7)}{R\text{-}(CN)_n} + \underset{(8)}{n\ R'\text{-COOH}} \qquad (\text{ I })$$

n = 1	1a, 6a	R = CH_3	n = 2	2a, 7a	R = CH_2
	b, b	$CH_3(CH_2)_3$		b, b	$(CH_2)_4$
	c, c	 $CH_2=C(CH_3)$		c, c	CH=CH
	d, d	C_6H_5		d, d	p-C_6H_4

3a, 8a R' = CH_3
b, b C_6H_5

The reaction scheme (I) shows the results we obtained from the reaction of a series of silylated aliphatic, olefinic, and aromatic mono- and diamides (1,2) with both acetic and benzoic acid chloride (3), see table 1:

Table 1

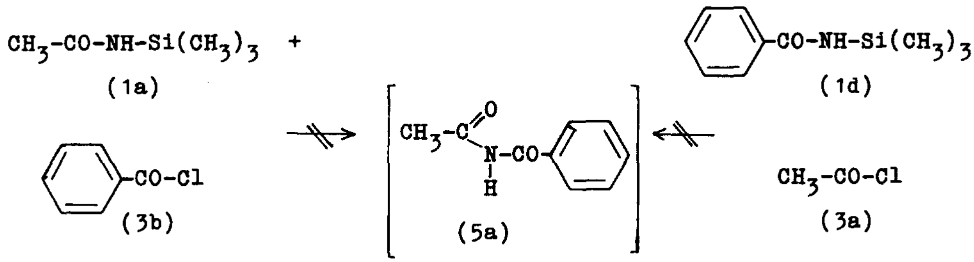
Conversion of N-trimethyl silylated amides (1,2) into nitriles (6,7)

Starting Materials	Yield %	of Compound	Starting Materials	Yield %	of Compound
1a + 3a	90	6a	2a + 3a	92	7a
1b + 3a	95	6b	2b + 3a	97	7b
1c + 3a	95	6c	2c + 3a	91	7c
1d + 3a	100	6d	2d + 3a	96	7d
1a + 3b	98	6a	2a + 3b	90	7a
1d + 3b	100	6d	2d + 3b	90	7d

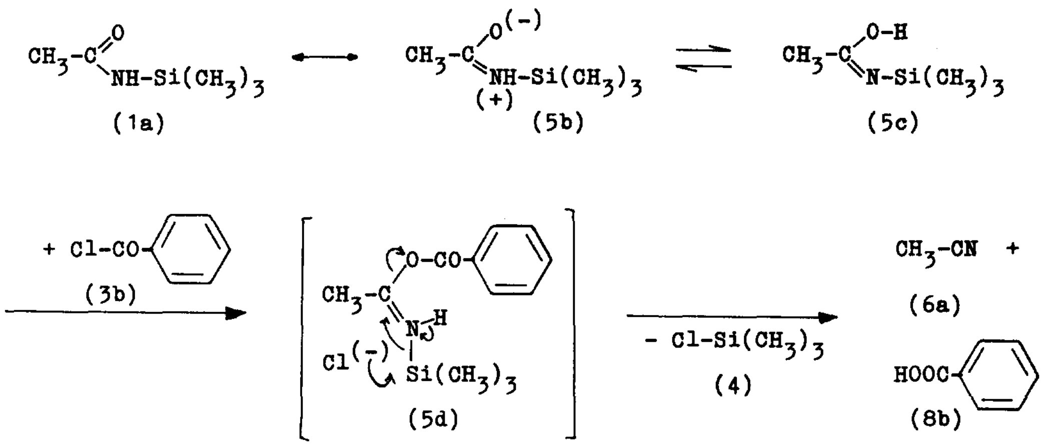
A detailed study by GIESSLER 3) of the tautomeric forms of a silylated amide, $RCONH_2$ and $RC(OH)=NH$, has shown that the product is the N-trimethyl silyl amide, $RCONHSi(CH_3)_3$ (where R = CH_3, C_2H_5, n-C_3H_7, Cl_3C, C_6H_5). O-Silylation may, in fact, occur first, with rapid tautomeric shift to the thermodynamically stable N-trimethyl silyl amide.

According to the structure of N-silylated amides presented by GIESSLER 3), both the reactions of N-trimethyl silyl acetamide (1a) with benzoyl chloride (3b) and of N-trimethyl silyl benzamide (1d) with acetyl chloride (3a) should lead to the same reactive intermediate (5a), which does not explain the easy decomposition into acetonitrile (6a) and benzoic acid (8b) and into benzonitrile (6d) and acetic acid (8a), respectively.

On the other hand the tautomeric forms (5b) and (5c) may play an important role as the reactive silylated molecules in which the O-atom is attacked by the acid chloride. The rearrangement of the unstable form (5d) with the loss of trimethyl chlorosilane (4) yields the nitrile and the acid almost quantitatively.



(II)



Our experiments have shown (see table 1) that in all the cases the silylated amide (1,2) is converted into the corresponding nitrile (6,7) independent of the chemical character of the N-trimethyl silylated amide.

This new reaction to convert an amide into the corresponding nitrile is applicable to any kind of amide as far as we found out. The choice of the acid chloride allows one to find the easiest separation of the reaction products.

Experimental Section.

Conversion of Acetamide into Acetonitrile:

Dry acetamide is silylated according to BIRKOFER et al. 1).

39.4 g (0.3 mole) N-trimethyl silyl acetamide (1a) and 42.0 g (0.3 mole) benzoyl chloride (3b) are heated in a flask fitted with distillation equipment. After the temperature has reached about 100°C, trimethyl chlorosilane (4) (bp. 54-5°C) starts to distil from the reaction mixture. The temperature is maintained until no more chlorosilane (4) distils. The next fraction obtained is acetonitrile (6a) (bp. 81-2°C) which is collected in 98 % yield. Benzoic acid (8b) remains in the flask.

References:

1) L.BIRKOFER, A.RITTER, and H.DICKOPP, Ber. 96 (1963) 1473

2) A.E.PIERCE, Silylation of Organic Compounds, Pierce Chemical Company, Rockford/Ill., USA, 1968

3) W.GIESSLER, Ph.D.Thesis, University of Cologne, Germany, 1963