A Journal of the Gesellschaft Deutscher Chemiker
Angewandte Chemie
GDCh
International Edition
www.angewandte.org

Accepted Article

Title: Facile synthesis of cyanide and isocyanides from CO

Authors: Douglas Wade Stephan, Maotong Xu, Bastiaan Kooij, Tongtong Wang, Jack H. Lin, Zheng-wang Qu, and Stefan Grimme

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202105909

Link to VoR: https://doi.org/10.1002/anie.202105909

WILEY-VCH

10.1002/anie.202105909

Facile synthesis of cyanide and isocyanides from CO

Maotong Xu[a], Bastiaan Kooij[a,b], Tongtong Wang[a,c], Jack H. Lin[a], Zheng-wang Qu[d*], Stefan Grimme,[d] Douglas W. Stephan[a*]

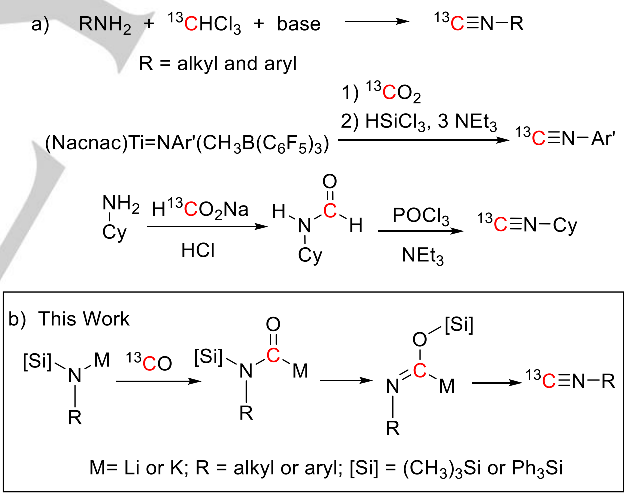
This work is dedicated to the memory of Professor Richard H. Holm.

a Mr. M. Xu, Mr. J.H. Lin, Professor Dr D.W. Stephan
Department of Chemistry, University of Toronto,
80 St. George St., Toronto, Ontario, Canada M5S3H6
Email: dstephan@chem.utoronto.ca
b. Mr. B. Kooij
Van 't Hoff Institute for Molecular Sciences, University of Amsterdam
1090 GD Amsterdam, The Netherlands
c. Ms. T. Wang
School of Chemistry, Faculty of Chemical, Environmental and Biological Science and Technology,
Dalian University of Technology, Dalian, 116023, China
d. Dr. Z.-W. Qu, Prof. Dr. Stefan Grimme
Mulliken Center for Theoretical Chemistry, Institut für Physikalische und Theoretische Chemie
Rheinische Friedrich-Wilhelms-Universität Bonn
Beringstrasse 4, 53115 Bonn, Germany
Email: qu@thch.uni-bonn.de

Electronic Supplementary Information (ESI) available: Synthetic and spectral data as well as DFT-computed energies and Cartesian coordinates are deposited. X-ray crystallographic data can be obtained from the CCDC 2080562-2080564.

Abstract: The reaction of $K[N(SiMe_3)_2]$ with ^{13}CO proceeds in C_6D_6 or THF affording $K^{13}CN$ and $O(SiMe_3)_2$ under mild conditions as confirmed by crystallographic characterization of K(18-crown-6)CN. Similarly reaction of the alkali metal amides, $M[N(SiR_3)R']$ (M= Li, K; R = Ph, Me; R′ = alkyl, aryl) provides the corresponding ^{13}C labeled isocyanide $RN^{13}C$ and $MOSiR_3$, generally in high yields. In some instances, the use of the sterically bulky Ph_3Si-substituent is required to preclude 1,2-silyl migration affording the silylcarbamoyl salt $M[Me_3SiC(O)NR']$. These reactions have been used to obtain 19 examples of ^{13}C labelled isocyanides, and several examples of gram scale reactions are reported. The mechanism of the reactions is probed via reliable DFT calculations.

Isocyanides (RNC) are versatile reagents in synthetic chemistry, acting as nucleophiles and electrophiles,[1] as well as participating in radical reactions.[2] This has led to applications in chemistry across the discipline. For example, isocyanides have been widely utilized in macromolecular[3] and polymer chemistry.[4] In more recent years, diastereomeric polyisocyanides[5], light-responsive polyisocyanides[6] and cross linked polyisocyanides[7] have been emerged. In bioorganic chemistry, isocyanides have been exploited for multicomponent reactions,[8] to prepare α-acyl carboxamides or dipeptides. In these cases, diastereoselective and enantioselective versions of these reactions[9] provide access to valuable products for drug discovery and development.[10] Isocyanides have also been exploited in biological chemistry as incorporation into amino acids provides opportunities for biorthogonal chemistry and protein labeling.[11] Isocyanides have also been extensively studied as ligands in coordination chemistry as they provide both a strong σ donor and π-acceptor properties. These features give rise to a variable coordination modes where isocyanides act as 2, 4 and 6 e^- donors,[12] and have been employed in transition metal complexes and main group chemistry.[13] In addition, isocyanides act as potent photo-reductants thus finding applications as photosensitizers.[14]



Scheme 1. (a) known routes to ^{13}C enriched isocyanides (b) schematic of the present chemistry. (Nacnac) = $[ArNC(tBu)]_2CH$, Ar' = 2,6-$iPr_2C_6H_3$, Cy = cyclohexyl

Given this broad utility and the convenience of ^{13}C NMR spectroscopy, it is perhaps surprising to note the paucity of synthetic routes to isotopically labelled $RN{\equiv}^{13}C$. Indeed, our survey of the literature revealed only a few synthetic routes. Mindiola and coworkers prepared a ^{13}C enriched aryl isocyanide from the stoichiometric reaction of a titanium−imide and $^{13}CO_2$ (Scheme 1a) in 2006.[15] In the same year, Kira and coworkers described the Si-C coupling reaction of a silylene and isocyanide and used the reaction of ^{13}C enriched chloroform with amines to prepare 2,6-$(iPr)_2C_6H_3N^{13}C$.[16] More recently, Yamashita used the same protocol to prepare $tBuN^{13}C$ for use in the examination of diborane reactivity.[17] In 2021, Islamova *et al*[18] synthesized cyclohexyl-N^{13}C from sodium ^{13}C-formate for use as a ligand in transition metal chemistry.

Targeting a facile route to ^{13}C enriched products, we noted our recent demonstration of reactions of both lithium amides and phosphides[19] with CO affording products with N-C and P-C bonds. Herein, we demonstrate the facile reactions of silylamides $M[N(SiMe_3)_2]$ and $M[N(SiR_3)R']$ (M= Li, K; R = Ph, Me; R′ = alkyl, aryl) with ^{13}CO provides convenient access to $^{13}CN^-$ and ^{13}C-labeled alkyl and aryl isocyanides. The mechanism of these reactions is discussed, and the protocol is adapted to gram scale syntheses.

In 1965, reaction of $Na[N(SiMe_3)_2]$, with CO at 80 °C and 100 atm pressure in petroleum ether or benzene was reported to give NaCN.[20] We began by examining the reaction of $K[N(SiMe_3)_2]$ in C_6D_6 with 1 atm pressure of CO in a J-young tube. No reaction was observed after 24 h at room temperature (Table 1, entry 1). However, heating to 50°C for 24 h, led to the formation of KCN in 64% yield (Table 1, entry 2), consistent with the appearance of the ^{13}C resonance at 166.6 ppm in D_2O and DMSO-d_6 and the concurrent appearance of the ^{1}H NMR resonance attributable to $O(SiMe_3)_2$. Repeating the reaction in THF at room temperature, affording K^{13}CN in 13% yield after 24 hours (Table 1, entry 3), however the yield improved to 89% at elevated temperature (50°C, Table 1, entry 4). Alternatively, elevating the pressure to 4 atm of ^{12}CO gave 78% yield after 24 h at room temperature (Table 1, entry 5). Under analogous conditions using $Li[N(SiMe_3)_2]$, Li^{13}CN was obtained in <1% yield (Table 1, entry 6). Addition of 18-crown-6 ether to $K[N(SiMe_3)_2]$ in THF at 50 °C, (Table 1, entry 7) led to poor reactivity. This was attributed to partially deprotonation of the crown ether by $K[N(SiMe_3)_2]$. However, this was avoided in THF or 1,4-dioxane at ambient temperature under 1 atm ^{13}CO. These reactions led to the formation of [(18-crown-6)K^{13}CN] **1** as colorless crystals after 24 h in 88 and 99% yields, respectively (Table 1, entry 8, 9). This optimized, mild protocol provides a facile route to isotopically labeled cyanide. We note that previous routes employed $^{13}CO_2$ and requires a Ru/Pt catalyst, H_2, NH_3 and forcing conditions.[21]

Table 1 Conditions for the formation of CN^- from CO and $M[N(SiMe_3)_2]$.

$$M[N(SiMe_3)_2] + {}^{13}CO \xrightarrow[\text{Temp}]{\text{Solvent}} M^{13}CN + (Me_3Si)_2O$$

Ent	Cation (M)	Solv	P (atm)	T (°C)	t (h)	Yield (%)
1[a]	K	C_6D_6	1	rt	24	<1[b]
2[a]	K	C_6D_6	1	50	24	64[b]
3	K	THF	1	rt	24	13[b]
4	K	THF	1	50	24	89
5[a]	K	THF	4	rt	24	78
6	Li	THF	1	rt	24	<1[b]
7	K(18-crown-6)	THF	1	50	5	<1[b]
8	K(18-crown-6)	THF	1	rt	24	88
9	K(18-crown-6)	1,4-dioxane	1	rt	24	>99[b]

[a] trial done with unlabelled CO. [b] yield determined by integration of the ^{1}H NMR spectrum.

A crystallographic study of **1** revealed its formulation as [K(18-crown-6)CN] with two molecules in the asymmetric unit. The K^+ ion is coordinated to six oxygen atoms of the crown with K-O distances falling in the range 2.76-2.97 Å. In addition, the K^+ ion is bound to a cyanide fragment with an average K-C distance of 2.70(1) Å and an average C-N bond distance of 1.07(1) Å (Figure 1). The K-C-N angle of is 130(1)º. These data affirm the remarkable and facile transformation of CO to CN^-.

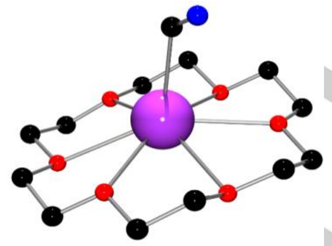
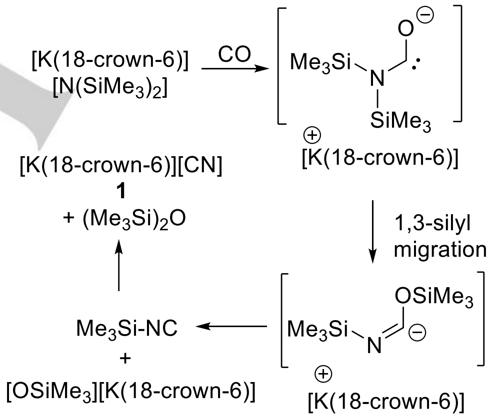


Figure 1 POV-ray depiction of one of the molecules in the asymmetric unit of **1**, hydrogen atoms are omitted for clarity. C: black, O: red, N: blue.

The formation of **1** presumably proceeds via nucleophilic attack of CO by amide generating a transient carbene species. Intramolecular 1,3-silyl group migration is followed by a 1,2 elimination of siloxide generating cyanide. A carbene-like intermediate was also proposed for the analogous reaction of the $[tBu_2P]^-$ anion with CO, where *t*Bu group migration from P to C afforded [K(18-crown-6)][*E*-*t*BuPC(*t*Bu)O].[19b] In the present case, silyl migration to oxygen is presumably thermodynamically favored by the strength of Si-O bonds.



Scheme 2 Proposed reaction pathway to **1**.

To further support the proposed mechanism, DFT calculations were performed at the PW6B95-D3/def2-QZVP + COSMO-RS // TPSS-D3/def2-TZVP + COMSO level of theory in THF solution.[22] Consistent with the known crystal structure,[23] the dimeric form of $[K(N(SiMe_3)_2)]_2$ is shown to be 1.9 kcal/mol more stable than the monomer in THF solution. Direct CO insertion into a K–N bond of $[K(N(SiMe_3)_2)]_2$ is 15.3 kcal/mol endergonic over a low free energy barrier of 16.5 kcal/mol (via transition state **TS1**) affords the transient intermediate **Int1.** Subsequently almost barrierless and highly exergonic 1,3-silyl-shift to cleave the C–O bond (via **TS2**) affords the complex $(Me_3Si)_2NK_2OSiMe_3$ and Me_3SiNC. Isomerization of isocyanide the cyanide Me_3SiCN is almost neutral in free energy but slow due to the barrier of 24.2 kcal/mol, with isocyanide being entropically favored on heating. Subsequent nucleophilic attack at the Si-center of Me_3SiNC by amide is −19.5 kcal/mol exergonic over a low barrier of 11.6 kcal/mol (via **TS3**) yielding the complex $(Me_3Si)_2NK_2CN$ and $O(SiMe_3)_2$. To this point, the reaction is highly

10.1002/anie.202105909

exergonic with a low overall barrier of 16.5 kcal/mol (**TS1**), and thus should be facile at room temperature. A very similar mechanism is also found for monomeric K(N(SiMe$_3$)$_2$ and CO, however this is kinetically 3.7 kcal/mol less favorable. The complex (Me$_3$Si)$_2$NK$_2$CN is further stabilized by −2.3 kcal/mol upon dimerization. The moderate yield of KCN observed experimentally suggests the possibility of the formation of higher amide-cyanide aggregates. Coordination of K$^+$ by 18-crown-6 stabilizes the monomeric potassium amide (18-crown-6)KN(SiMe$_3$)$_2$ by −7.4 kcal/mol and kinetically favors reaction with CO by 1.8 kcal/mol (see ESI). The corresponding reaction using [(THF)LiN(SiMe$_3$)$_2$]$_2$ encounters a 4.9 kcal/mol higher barrier (21.4 kcal/mol via **TS1Li**, see ESI) due to stronger THF coordination and less ionic Li–N amide bond.

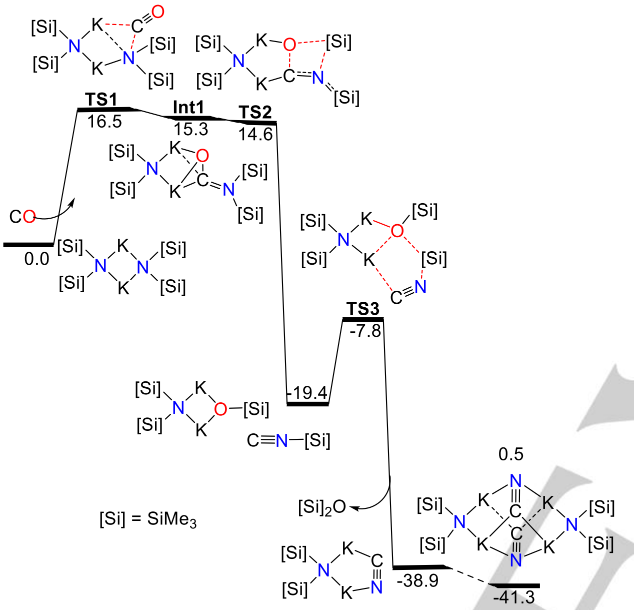


Figure 2 DFT-computed free energy path (in kcal/mol, 298 K) from CO to CN$^-$.

The mechanism infers the formation of intermediates Me$_3$SiNC with KOSiMe$_3$ suggesting substituted-silyl amides could provide isocyanides. To that end, the silylamide [(Me$_3$Si)(*t*Bu)N]K was prepared via deprotonation of the corresponding amine with one equivalent of benzyl potassium in THF. Subsequent reaction with ^{13}CO (1 atm) at room temperature for 12 h, led to the immediate discoloration of the solution and the quantitative conversion to *t*BuN^{13}C **2** and Me$_3$SiOK as evidenced by the ^{13}C resonance at 155.1 ppm (Table 2, entry 1). Similarly, using 1 atm ^{13}CO with [(Me$_3$Si)(*t*Bu)N]Li, the isotopically labeled isocyanide *t*BuN^{13}C **2** was obtained in 98% yield **(**Table 2, entry 2).

To probe the generality of this reactivity, a series of silylamides [(Me$_3$Si)(R)N]M (M = Li, K) were prepared. The silylamide [(Me$_3$Si)(Ad)N]Li (Ad = adamantyl) gave AdN^{13}C **3** in 81% yield (Table 2, entry 3). Analogous reactions of arene substituted amides [(Me$_3$Si)(Ar)N]Li (Ar = 2-*i*PrC$_6$H$_4$, 2-PhC$_6$H$_4$, 2-Me-4-MeOC$_6$H$_3$, 2,6-Me$_2$C$_6$H$_3$, 2,6-*i*Pr$_2$C$_6$H$_3$, 2,4,6-(*t*Bu)$_3$C$_6$H$_2$, 2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$) gave the corresponding isotopically enriched isocyanides **4-10** in yields ranging from 71 to 97% (Table 2 Entry 4-10).

In the reaction of the sterically less demanding [(Me$_3$Si)(4-MeOC$_6$H$_4$)N]Li, while the isocyanide was the major product as evidenced in the ^{13}C{^{1}H} NMR triplet ($^1J_{C\text{-}N}$ = 5 Hz) at 164 ppm, another signal at 180 ppm exhibited ^{29}Si satellites with $^1J_{C\text{-}Si}$ = 60 Hz was consistent with the formation of the carbamoyl lithium species, [(Me$_3$Si)C(O)N(4-MeOC$_6$H$_4$)]Li consistent with previous reports of silylation of amidocarbomoyl lithium species.[24] In the present case, these two species were present in a ratio of 2:1 (Table 2, entry 11), indicating that 1,3 and 1,2 silyl migrations are energetically competitive. To sterically favor 1,3 migration of the silyl group to oxygen the amide [(Ph$_3$Si)(4-MeOC$_6$H$_4$)N]K was reacted with CO. After 12 h, the isocyanide formed in quantitative yield (Table 2, entry 12). In a similarly fashion, Ph$_3$Si-derived amides afforded the alkyl isocyanides RNC (R = iPr **12**, Bu **13**, hexyl **14**) in good yields (Table 2, entry 13-15). In addition, the aryl isocyanides RNC (C$_6$H$_5$ **15**, 3-MeOC$_6$H$_4$ **16**, 4-Me$_2$NC$_6$H$_4$ **17**, 4-PhOC$_6$H$_4$ **18**, 4-*i*PrC$_6$H$_4$ **19**) were formed in yields of 74-95% (Table 2, entry 16-20). Efforts to apply this protocol to picolyl substituted silylamide led to known cyclization affording imidazo[1, 5-*a*]pyridine-3-^{13}C **20**, via the transient isocyanide intermediate.[25]

Table 2 Conditions for the formation of RN^{13}C from ^{13}CO and M[N(SiR'$_3$)R].

$$\mathrm{M[N(SiR'_3)R]} + \underset{(1\ \mathrm{atm})}{^{13}\mathrm{CO}} \xrightarrow[\text{rt, 12 h}]{\text{THF}} \mathrm{RN^{13}C} + \mathrm{R'_3SiOM}$$

Ent	R'	[Si]	M	Yield (%)[a]	RN^{13}C
1	*t*Bu	Me$_3$Si	K	> 99[b]	**2**
2	*t*Bu	Me$_3$Si	Li	98	**2**
3	Adamantyl	Me$_3$Si	Li	81	**3**
4	2-*i*PrC$_6$H$_4$	Me$_3$Si	Li	93	**4**
5	2-PhC$_6$H$_4$	Me$_3$Si	K	71	**5**
6	2-Me-4-OMeC$_6$H$_3$	Me$_3$Si	Li	95	**6**
7	2,6-Me$_2$C$_6$H$_3$	Me$_3$Si	Li	97	**7**
8	2,6-*i*Pr$_2$C$_6$H$_3$	Me$_3$Si	Li	93	**8**
9[d]	2,4,6-(*t*Bu)$_3$C$_6$H$_2$	Me$_3$Si	Li	86[c]	**9**
10	2,6-(Ph$_2$CH)$_2$-4-Me C$_6$H$_2$	Me$_3$Si	Li	92	**10**
11	4-MeOC$_6$H$_4$	Me$_3$Si	Li	66[e]	**11**
12	4-MeOC$_6$H$_4$	Ph$_3$Si	K	99	**11**
13	*i*Pr	Ph$_3$Si	Li	98	**12**
14	Bu	Ph$_3$Si	K	89	**13**
15	Hexyl	Ph$_3$Si	K	97	**14**
16	C$_6$H$_5$	Ph$_3$Si	K	74	**15**
17	3-MeOC$_6$H$_4$	Ph$_3$Si	K	86	**16**
18	4-Me$_2$NC$_6$H$_4$	Ph$_3$Si	K	95	**17**
19	4-PhOC$_6$H$_4$	Ph$_3$Si	K	87	**18**
20	4-*i*PrC$_6$H$_4$	Ph$_3$Si	K	88	**19**
21[d]	2-Picolyl	Ph$_3$Si	Li	91[c]	**20**

[a]yield determined by ^{13}C{^{1}H} NMR spectroscopy using [^{13}C] urea as internal standard; [b]yield determined by ^{1}H NMR spectroscopy; [c]isolated yield; [d]36 h; [e]yield determined by relative integration of isocyanide: carbamoyl species.

In the case of the isocyanides RNC (R = 2,6-(*i*Pr)$_2$C$_6$H$_3$ **8**; 2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$ **10**), cocrystalization of reaction products afforded crystals of the tetra-lithium-siloxide clusters formulated as [(2,6-(*i*Pr)$_2$C$_6$H$_3$NCLiOSiMe$_3$)]$_4$ and [(THF)$_2$(2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$)NC)$_2$(LiOSiMe$_3$)$_4$], respectively (Figure 3a, b). Both species are LiOSiMe$_3$ pseudo-cubanes where oxygen atoms bridge the lithium atoms. The coordination spheres of the Li-atoms are completed with either an isocyanide or THF molecule. Presumably, the steric bulk of the latter isocyanide precludes the inclusion of four isocyanides about the Li-O cluster, prompting THF coordination. The Li-C distances were 2.243(4) and 2.258(17) Å for R = 2,6-(*i*Pr)$_2$C$_6$H$_3$ and 2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$, respectively, with N-C distances being 1.154(3) and 1.161(11) Å, respectively. In the case of, 2,4,6-(*t*Bu)$_3$C$_6$H$_2$NC **9**, its differing solubility allowed crystallization of the isocyanide in the absence of the Li-siloxide (Figure 3c). The N-C distance was 1.159(4) Å.

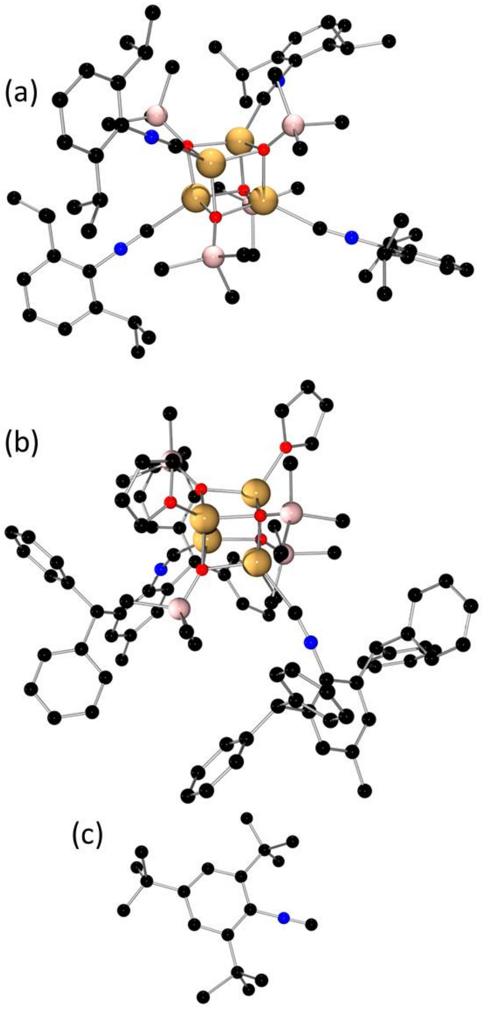
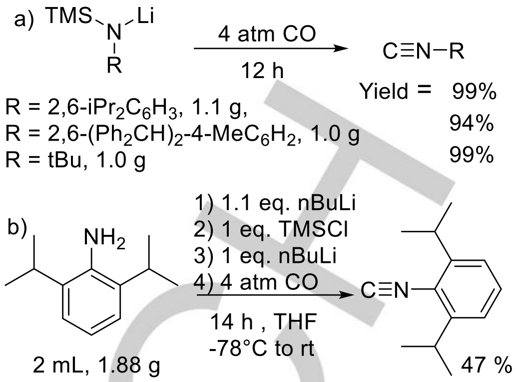


Figure 3 POV-ray depictions of the crystal structures of (a) [(2,6-(iPr)$_2$C$_6$H$_3$NCLiOSiMe$_3$)]$_4$, (b) [(THF)$_2$(2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$)NC)$_2$(LiOSiMe$_3$)$_4$], and (c) 2,4,6-(tBu)$_3$C$_6$H$_2$NC. Hydrogen atoms are omitted for clarity, C: black, N: blue, O: red, Si: pink, Li: bronze.

Several examples of these syntheses were performed on a gram scale. Reactions of 1.1 g of [(Me$_3$Si)(2,6-iPr$_2$C$_6$H$_3$)N]Li or 1.0 g of [(Me$_3$Si)(2,6-(Ph$_2$CH)$_2$-4-MeC$_6$H$_2$)N]Li in THF with CO afforded the corresponding isocyanides in isolated yields 99 and 94% after recrystallization (Scheme 3), respectively. Similarly, 1 g of [(Me$_3$Si)(tBu)N]Li in C$_6$D$_6$ led to quantitative conversion to tBuNC, as evidenced by ^{1}H NMR spectrum. Efforts to develop a one-pot synthesis from the parent amines were also probed. Using 1.88 g of 2,6-iPr$_2$C$_6$H$_3$NH$_2$ successive additions of 1.1 equivalent of nBuLi, 1 equivalent of Me$_3$SiCl, and a second equivalent of nBuLi and CO for 12 h in THF afforded the isocyanide 2,6-iPr$_2$C$_6$H$_3$NC in 47% isolated yield (Scheme 3).



Scheme 3 Examples of gram-scale and one-pot reactions to isocyanides.

In conclusion, the reaction of silylamides with CO provides a facile and low-pressure protocol to both KCN and isocyanides. Understanding the mechanism using reliable DFT calculations has allowed the adaptation of this reaction to the preparation of a series of 19 isocyanides. This methodology is readily adapted to the inclusion of ^{13}C isotopic labeling at the cyano or isocyanide carbons. In addition, it is shown to be viable in gram scale preparations. We are continuing to explore the reaction chemistry of alkali-metal species with small molecules.

Acknowledgements

D.W.S. is grateful to NSERC of Canada for research support and the award of an NSERC Canada Research Chair and to the Guggenheim Foundation for a 2020 Guggenheim Fellowship and Killam foundation for the 2021 Killam Prize. Z.W.Q and S.G are grateful to DFG (project SPP1807 and Gottfried Wilhelm Leibnitz prize to S.G) for financial support. M.X. is grateful for the award of Colin H. Bayley Scholarship. T.W. is grateful to China Scholarship Council for financial support.

Keywords: Cyanide • carbon monoxide • isotopic labelling • small molecule activation• ^{13}C labelled iso cyanides

[1] R. M. Wilson, J. L. Stockdill, X. Wu, X. Li, P. A. Vadola, P. K. Park, P. Wang, S. J. Danishefsky, *Angew. Chem. Int. Ed.* **2012**, *51*, 2834-2848.
[2] D. P. Curran, H. Liu, *J. Am. Chem.Soc.* **1991**, *113*, 2127-2132.
[3] (a) D. G. Rivera, L. A. Wessjohann, *J. Am. Chem. Soc.* **2006**, *128*, 7122-7123; (b) T. Tian, R. Hu, B. Z. Tang, *J. Am. Chem. Soc.* **2018**, *140*, 6156-6163.
[4] (a) E. Schwartz, M. Koepf, H. J. Kitto, R. J. M. Nolte, A. E. Rowan, *Polym. Chem.* **2011**, *2*, 33-47; (b) F. Millich, *Chem. Rev.* **1972**, *72*, 101-113; (c) T. J. Deming, B. M. Novak, *J. Am. Chem. Soc.* **1993**, *115*, 9101-9111; (d) R. J. M. Nolte, A. J. M. v. Beijnen, W. Drenth, *J. Am. Chem. Soc.* **1974**, *96*, 5932-5933.
[5] T. Kajitani, K. Okoshi, S.-I. Sakurai, J. Kumaki, E. Yashima, *J. Am. Chem. Soc.* **2006**, *128*, 708-709.
[6] S. K. Pomarico, C. Wang, M. Weck, *Macromol Rapid Comm* **2020**, *41*, 1900324.
[7] (a) S. K. Pomarico, D. S. Lye, E. Elacqua, M. Weck, *Polymer Chemistry* **2018**, *9*, 5655-5659; (b) Q. Wang, J. Huang, Z.-Q. Jiang, L. Zhou, N. Liu, Z.-Q. Wu, *Polymer* **2018**, *136*, 92-100.
[8] I. Ugi, *Angew. Chem. Int. Ed.* **1962**, *1* 8-21.
[9] (a) D. J. Ramón, M. Yus, *Angew. Chem. Int. Ed.* **2005**, *44*, 1602-1634; (b) J. Zhang, P. Yu, S.-Y. Li, H. Sun, S.-H. Xiang, J. Wang, K. N. Houk, B. Tan, *Science* **2018**, *361*, eaas8707.
[10] P. Slobbe, E. Ruijter, R. V. A. Orru, *MedChemComm* **2012**, *3*, 1189.
[11] Y. Chen, K.-L. Wu, J. Tang, A. Loredo, J. Clements, J. Pei, Z. Peng, R. Gupta, X. Fang, H. Xiao, *ACS Chem. Bio.* **2019**, *14*, 2793-2799.
[12] F. P. Pruchnik, S. A. Duraj, in *Organometallic Chemistry of the Transition Elements* (Eds.: F. P. Pruchnik, S. A. Duraj), Springer, Boston MA, **1990**.

[13] (a) M. J. Drance, J. D. Sears, A. M. Mrse, C. E. Moore, A. L. Rheingold, M. L. Neidig, J. S. Figueroa, *Science* **2019**, *363*, 1203-1205; (b) J. S. Figueroa, J. G. Melnick, G. Parkin, *Inorg. Chem.* **2006**, *45*, 7056-7058; (c) B. R. Barnett, C. E. Moore, A. L. Rheingold, J. S. Figueroa, *J. Am. Chem. Soc.* **2014**, *136*, 10262-10265; (d) R. B. Brandon, C. Moore, E., A. Rheingold, L., J. Figueroa, S., *Chem. Commun.* **2015**, *51*, 541-544; (e) J. Böhnke, H. Braunschweig, T. Dellermann, W. C. Ewing, T. Kramer, I. Krummenacher, A. Vargas, *Angew. Chem. Int. Ed.* **2015**, *54*, 4469-4473; (f) T. J. Hadlington, T. Szilvasi, M. Driess, *Chem. Sci.* **2018**, *9* 2595–2600.

[14] W. Sattler, M. E. Ener, J. D. Blakemore, A. A. Rachford, P. J. Labeaume, J. W. Thackeray, J. F. Cameron, J. R. Winkler, H. B. Gray, *J. Am. Chem. Soc.* **2013**, *135*, 10614-10617.

[15] U. J. Kilgore, F. Basuli, J. C. Huffman, D. J. Mindiola, *Inorg. Chem.* **2006**, *45*, 487-489.

[16] (a) H. Asakawa, K.-H. Lee, Z. Lin, M. Yamashita, *Nat Commun* **2014**, *5*; (b) T. Abe, T. Iwamoto, C. Kabuto, M. Kira, *J. Am. Chem. Soc.* **2006**, *128*, 4228-4229.

[17] Y. Katsuma, N. Tsukahara, L. Wu, Z. Lin, M. Yamashita, *Angew. Chem. Int. Ed.* **2018**, *57*, 6109-6114.

[18] M. V. Dobrynin, E. V. Sokolova, M. A. Kinzhalov, A. S. Smirnov, G. L. Starova, V. Y. Kukushkin, R. M. Islamova, *ACS Applied Polymer Materials* **2021**, *3*, 857-866.

[19] (a) M. T. Xu, A. R. Jupp, Z. W. Qu, D. W. Stephan, *Angew. Chem. Int. Ed.* **2018**, *57*, 11050-11054; (b) M. T. Xu, A. R. Jupp, D. W. Stephan, *Angew. Chem. Int. Ed.* **2019**, *58*, 3548-3552; (c) M. Xu, Z.-W. Qu, S. Grimme, D. W. Stephan, *J. Am. Chem. Soc.* **2021**, *143*, 634-638.

[20] U. Wannagat, H. Seyffert, *Angew. Chem. Int. Ed.* **1965**, *4*, 438-439.

[21] D. G. Ott, V. N. Kerr, T. G. Sanchez, T. W. Whaley, *Journal of Labelled Compounds and Radiopharmaceuticals* **1980**, *17*, 255-262.

[22] (a) *Vol. See http://www.turbomole.com~~.~~*, TURBOMOLE GmbH, Karlsruhe, **2018**; (b) J. Tao, J. P. Perdew, V. N. Staroverov, G. E. Scuseria, *Phys Rev Lett* **2003**, *91*; (c) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104; (d) S. Grimme, S. Ehrlich, L. Goerigk, *Journal of Computational Chemistry* **2011**, *32*, 1456-1465; (e) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297-3305; (f) A. Klamt, G. Schüürmann, *J. Chem. Soc. Perkin Trans.* **1993**, *2*, 799; (g) F. Weigend, *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057-1065; (h) S. Grimme, *Chem. Eur. J.* **2012**, *18*, 9955-9964; (i) F. Eckert, A. Klamt, *AIChE J.* **2002**, *48*, 369-385; (j) F. Eckert, A. Klamt, COSMOlogic GmbH & Co., Leverkusen, Germany, **2015**; (k) Y. Zhao, D. G. Truhlar, **2005**, *109*, 5656-5667.

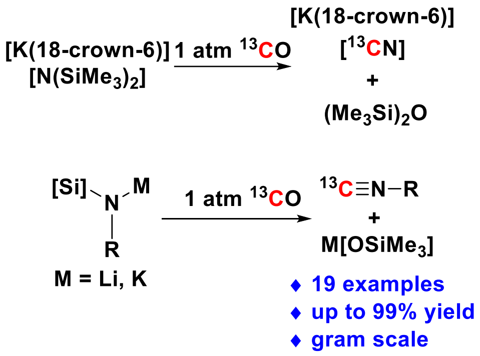
[23] K. F. Tesh, T. P. Hanusa, J. C. Huffman, *Inorg. Chem.* **1990**, *29*, 1584–1586.

[24] (a) A. Orita, K. Ohe, S. Murai, *Organometallics* **1994**, *13*, 1533-1536; (b) D. Seyferth, R. M. Weinstein, *J. Am. Chem. Soc.* **1982**, *104*, 5534-5535.

[25] U. Schollkopf, E. Eilers, K. Huntke, *Liebigs Ann. Chem.* **1976**, 969-977.

Entry for the Table of Contents

Insert graphic for Table of Contents here. ((Please ensure your graphic is in **one** of following formats))



The reactions of K[N(SiMe$_3$)$_2$] with ^{13}CO affords K^{13}CN and O(SiMe$_3$)$_2$ under mild conditions. DFT calculations affirmed this reaction proceeds via an isocyanide intermediate. This was confirmed experimentally as the alkali metal amides, M[N(SiR$_3$)R′] (M= Li, K; R = Ph, Me; R′ = alkyl, aryl) are shown to provide a facile route to the 19 ^{13}C labeled isocyanide RN^{13}C and MOSiR$_3$ generally in high yields.

researcher Twitter usernames: @FLPchemist