Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2009, **19**, 281–283
Mendeleev Communications

Cyanomethylamines and azidomethylamines: new general methods of the synthesis and transformations†

Orudzh G. Nabiev, Zargalam O. Nabizade and Remir G. Kostyanovsky*

N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 495 651 2191; e-mail: kost@chph.ras.ru

DOI: 10.1016/j.mencom.2009.09.018

Simple and efficient methods have been developed to obtain cyanomethylamines and azidomethylamines using reactions of methoxymethylamines with TMSCN and $TMSN_3$, respectively. In the case of dimethylformamide dimethylacetal, only one MeO group was substituted with CN, and an unexpected direction of the subsequent azidation was found. Adducts of azidomethylamines with DMAD were studied, and the base-catalyzed isomerization of symmetric triazoles into non-symmetric ones was revealed.

Long-time investigations in the chemistry of cyanomethylamines[1(*b*),2] and azidomethylamines[3] provided a number of useful reagents, synthons and valuable materials (including energetics).

The idea of this work is to use commercial reagents TMSCN and $TMSN_3$ both of which have strong nucleophile groups, CN and N_3, in order to synthesize cyanomethylamines **2** and azidomethylamines **3**, respectively, by aminomethylation with alkoxymethylamines **1** (Scheme 1).

$$\underset{\mathbf{2}}{R_2NCH_2CN} \xleftarrow[-\,TMSOR]{TMSCN} \underset{\mathbf{1}}{R_2NCH_2OR} \xrightarrow[-\,TMSOR]{TMSN_3} \underset{\mathbf{3}}{R_2NCH_2N_3}$$

Scheme 1

Possibilities of such an approach are confirmed by the earlier reported data on the cyanation of methoxymethylamines with $TMSCN/Et_2O{\cdot}BF_3$,[1(*b*)] syntheses of cyanomethylamines[2(*a*)] and azidomethylamines[3(*a*)] by reactions of iminium salts with Na and Ag cyanides and azides, as well as cyanosilylation of aldehydes and ketones under the action of TMSCN.[4] We have accomplished the azidosilylation of bromal [in Et_2O, 24 h, at 20 °C, ^{1}H NMR ($CDCl_3$) δ: 0.33 (s, 9H, Me_3Si), 8.54 (s, 1H, HC)] (Scheme 2).

$$CBr_3CH{=}O + Me_3SiN_3 \longrightarrow CBr_3CH\begin{matrix}N_3\\OSiMe_3\end{matrix}$$

Scheme 2

The smooth azidation of Me_3N with a combination of PhIO/$TMSN_3$[3(*f*)] can be explained by its oxidation to Me_2NCH_2OH followed by aminomethylation of $TMSN_3$.

Starting alkoxymethylamines **1**‡ were prepared from the corresponding amines and polyoxymethylene in MeOH according to the known methods[5] and used for the syntheses of cyanomethylamines **2** and azidomethylamines **3** (Table 1).§,¶

Cyanomethylamines were characterized by NMR, MS (ions $M^{+\cdot}$ and $M - CN^+$ are observed), and IR spectra (2020–2040 cm^{-1}).§

Azidomethylamines were characterized by NMR, MS (ions $M^{+\cdot}$ and $M - N_3^+$ are observed), UV (245–250 nm) and IR spectra [2100–2110 cm^{-1}, *cf.* ref. 3(*g*)].¶

It was found that in the course of cyanation and azidation of dimethylformamide dimethylacetal **4**, only one MeO group is substituted. Upon subsequent azidation, stable cyanation product **5** undergoes spontaneous fragmentation like unstable methoxyazide. Thus, despite expectations, azidation of **5** results in the substitution of CN group rather than MeO group, accompanied with spontaneous fragmentation into MeN_3 and DMF (Scheme 3).

Methylazide was isolated and characterized by ^{1}H NMR spectrum ($CDCl_3$) δ: 3.00 (s) [*cf.* ref. 3(*e*)] and its transformation into triazole **6** (Scheme 4).

† Geminal systems. Part 58. Previous communication, see ref. 1(*a*).

‡ NMR spectra were measured on a Bruker WM-400 spectrometer (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C), mass spectra, on a Bruker spectrospin CMS-47 spectrometer with electrospray ionization, IR spectra, on Perkin–Elmer RX-1000 and UV spectra, on a Specord UV/VIS spectrophotometer.

1a: yield 33%, bp 63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.4 (s, 6H, Me_2N), 3.35 (s, 3H, MeO), 3.97 (s, 2H, NCH_2O).

1b: yield 89%, bp 88–90 °C (1 Torr), $[\alpha]_D^{20}$ +42.46 (*c* 3.02, MeOH). ^{1}H NMR ($CDCl_3$) δ: 1.4 (d, 3H, *Me*CH, ^3J 6.7 Hz), 2.4 (s, 3H, MeN), 3.24 (s, 3H, MeO), 3.86 (q, 1H, HC, ^3J 6.7 Hz), 4.1 (2H, OCH_2N, AB-spectrum, $\Delta\nu$ 94.4 Hz, ^2J –9.2 Hz), 7.32 (m, 5H, Ph).

1c: yield 34.5%, bp 34–36 °C (15 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.77 (tt, 4H, CCH_2CH_2C), 2.76 (t, 4H, CH_2NCH_2), 3.31 (s, 3H, MeO), 4.14 (s, 2H, NCH_2O). MS, *m*/*z*: 503.1605 $[M + Na]^+$; calc. for M^+: 480.172.

1d: yield 65.5%, bp 66–67 °C (36 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.68, 1.76, 2.75 [10H, $(CH_2)_5N$], 3.30 (s, 3H, MeO), 4.12 (s, 2H, NCH_2O).

1e: yield 43%, bp 96–98 °C (6 Torr). ^{1}H NMR ($CDCl_3$) δ: 2.73 [s, 8H, $N(CH_2CH_2)_2N$], 3.3 (s, 6H, 2MeO), 4.0 (s, 4H, $2OCH_2N$).

1f: yield 53%, bp 81 °C (1 Torr). ^{1}H NMR ($CDCl_3$) δ: 3.27 (s, 6H, 2MeO), 4.0 (s, 2H, CH_2Ph), 4.24 (s, 4H, $2CH_2O$), 7.3 (m, 5H, Ph).

1g: yield 66%, bp 122–124 °C (1 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.6, 1.67, 1.78, 1.79, 2.04 (15H, Ad), 3.18 (s, 6H, MeO), 4.36 (s, 4H, NCH_2O).

1h: yield 54%, bp 105–107 °C (4 Torr). ^{1}H NMR ($CDCl_3$) δ: 1.25 (t, 3H, CMe), 3.34 (s, 3H, MeO), 3.51 (q, 2H, CH_2C), 4.73 (s, 2H, NCH_2O), 6.88 (m, 5H, Ph).

1i: yield 53%, bp 86–88 °C (4 Torr). ^{1}H NMR ($CDCl_3$) δ: 2.41 (s, 6H, NMe_2), 4.08 (s, 2H, OCH_2N), 4.53 (s, 2H, OCH_2O), 4.53 (s, 2H, $PhCH_2$), 7.34 (m, 5H, Ph).

§ *General procedure.* To a stirred Et_2O solution of methoxymethylamine equimolar quantity of TMSCN (CAUTION: Toxic!) was added and the solution was left for 10–12 h at 20 °C. After evaporation of the solvent the solid product (**2e**) was separated or liquid (**2a**,**b**) was distilled in a vacuum.

2a: bp 66–68 °C (80 Torr). ^{1}H NMR ($CDCl_3$) δ: 2.35 (s, 6H, Me_2N), 3.49 (s, 2H, NCH_2CN).

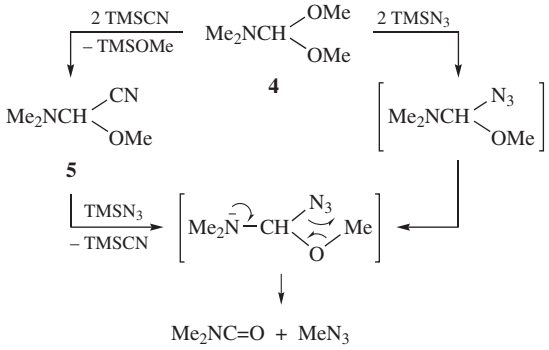
2b: bp 105–107 °C (1 Torr), $[\alpha]_D^{20}$ +132 (*c* 1.4, MeOH). ^{1}H NMR ($CDCl_3$) δ: 1.39 (d, 3H, *Me*CH, ^3J 6.7 Hz), 2.4 (s, 3H, MeN), 3.46 (2H, CH_2CN, AB-spectrum, $\Delta\nu$ 56 Hz, ^2J –17.2 Hz), 3.49 (q, 1H, HC, ^3J 6.7 Hz), 7.32 (m, 5H, Ph).

2e: mp 58–60 °C. ^{1}H NMR ($CDCl_3$) δ: 2.66 [s, 8H, $N(CH_2CH_2)_2N$], 3.54 (s, 2H, NCH_2CN).

Table 1 Synthesis of cyanomethylamines **2** and azidomethylamines **3** by reaction of methoxymethylamines **1** with TMSCN and $TMSN_3$, respectively.

$R^1R^2NCH_2OMe$	Products	
	$R^1R^2NCH_2CN$ (yield, %)	$R^1R^2NCH_2N_3$ (yield, %)
1a $R^1 = R^2 = Me$	**2a**[a] (94)	**3a**[b] (95)
(*R*)-(+)-**1b** $R^1 = Me$, $R^2 = CHMePh$	(*R*)-(+)-**2b** (94)	(*R*)-(+)-**3b** (95)
1c $R^1 + R^2 = (CH_2)_4$	—	**3c** (92)
1d $R^1 + R^2 = (CH_2)_5$	—	**3d** (93)
1e $R^1 + R^2 = (CH_2)_2NCH_2(OMe)(CH_2)_2$	**2e** (94)	**3e** (91.5)
1f $R^1 = CH_2OMe$, $R^2 = CH_2Ph$	—	**3f** $R^1 = CH_2N_3$, $R^2 = CH_2Ph$ (90)
1g $R^1 = CH_2OMe$, $R^2 = Ad$	—	**3g** $R^1 = CH_2N_3$, $R^2 = Ad$ (89)
1h $R^1 = Et$, $R^2 = Ph$	—	**3h** (95)

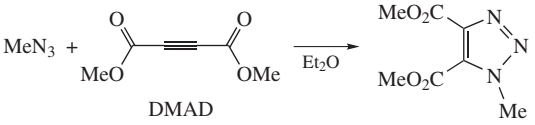
[a]Compound **2a** was also obtained by reaction of $Me_2NCH_2OCH_2OCH_2Ph$ (**1i**) with TMSCN. [b]Compound **3a** was also obtained by reaction of **1i** with $TMSN_3$.



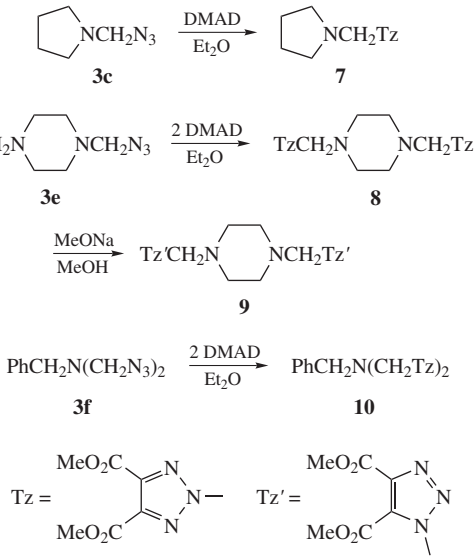
Scheme 3

Synthetic perspectives of azidomethylamines were demonstrated by reactions of [3 + 2] cycloaddition of **3c**,**e**,**f** to dimethyl acetylenedicarboxylate (DMAD), and the base-catalyzed rearrangement of symmetric triazole **8** into non-symmetric triazole **9** was found (Scheme 5).††

Data on the structures of **3e** and **10** in crystals and **3a**,**c** and **5** in gas phase will be published elsewhere.



Scheme 4



Scheme 5

This work was supported by the Russian Academy of Sciences and the Russian Foundation for Basic Research (grant no. 09-03-00537-a).

References

1 (*a*) V. G. Shtamburg, O. V. Shishkin, R. I. Zubatyuk, S. V. Kravchenko, A. V. Tsygankov, V. V. Shtamburg, V. B. Distanov and R. G. Kostyanovsky, *Mendeleev Commun*., 2007, **17**, 178; (*b*) T. Chiba, I. Saitoh, M. Okimoto, T. Tanase and S. Yano, *J. Org. Chem*., 1999, **64**, 2516.

2 (*a*) D. Enders and J. P. Shilvock, *Chem. Soc. Rev*., 2000, **29**, 359; (*b*) E. Leclere, E. Vrancken and P. Mangeney, *J. Org. Chem*., 2002, **67**, 8928; (*c*) H. P. Husson and J. Royer, *Chem. Soc. Rev*., 1999, **28**, 383; (*d*) A. Peroza, M. Selva and P. Tundo, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1033; (*e*) M. Bejaud, L. Mion and A. Commeyras, *Tetrahedron Lett*., 1975, **34**, 2985.

¶ **3a**: bp 110 °C. ^1H NMR ($CDCl_3$) δ: 2.41 (s, 6H, Me_2N), 4.31 (s, 2H, NCH_2N_3). $^{13}C\{^1H\}$ NMR (100.61 MHz, $CDCl_3$) δ: 41.31 (Me_2N), 76.90 (NCH_2N_3).

3b: bp 110–112 °C (1 Torr), $[\alpha]_D^{20}$ +27 (*c* 1.18, MeOH). ^1H NMR ($CDCl_3$) δ: 1.38 (d, 3H, *Me*CH, ^3J 6.7 Hz), 2.42 (s, 3H, MeN), 3.75 (q, 1H, HC, ^3J 6.7 Hz), 4.37 (dd, 2H, NCH_2N_3, AB-spectrum, $\Delta\nu$ 88.2 Hz, ^2J –8.6 Hz), 7.32 (m, 5H, Ph).

3c: bp 53–55 °C (10 Torr). ^1H NMR ($CDCl_3$) δ: 1.79, 1.82 [tt, 4H, $C(CH_2)_2C$], 2.78, 2.81 (t, 4H, CH_2NCH_2), 4.48 (s, 2H, NCH_2N_3), $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 23.9 [$C(CH_2)_2C$], 49.07 (CH_2NCH_2), 71.44 (NCH_2N_3).

3d: bp 73–74 °C (10 Torr). ^1H NMR ($CDCl_3$) δ: 1.71, 1.79, 2.79 [10H, $(CH_2)_5N$], 4.49 (s, 2H, NCH_2N_3).

3e: mp 109–110 °C. ^1H NMR ($CDCl_3$) δ: 2.74 [s, 8H, $N(CH_2CH_2)_2N$], 4.32 (s, 4H, $2NCH_2N_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 48.76 [s, $N(CH_2CH_2)_2N$], 75.17 (s, NCH_2N_3). ICR (electrospray ionization) MS, *m*/*z*: 197.1266 $[M + H]^+$; calc. for M^+: 196.119.

3f: bp 102–103 °C (1 Torr). ^1H NMR ($CDCl_3$) δ: 3.97 (s, 2H, PhCH_2N), 4.36 (s, 4H, $2NCH_2N_3$), 7.35 (m, 5H, Ph). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 53.35 (s, CH_2Ph), 70.05 (s, NCH_2N_3), 127.51, 128.58, 135.98 (Ph).

3g: mp 68–69 °C. ^1H NMR ($CDCl_3$) δ: 1.64, 1.68, 1.78, 2.13 (15H, Ad), 4.55 (s, 4H, NCH_2N_3).

3h: bp 115–117 °C (2 Torr). ^1H NMR ($CDCl_3$) δ: 1.27 (t, 3H, MeC), 3.53 (q, 2H, CH_2C), 4.88 (s, 2H, NCH_2N_3), 7.26 (m, 5H, Ph).

†† **5**: yield 96%, bp 90–92 °C (80 Torr). ^1H NMR ($CDCl_3$) δ: 2.35 (s, 6H, Me_2N), 3.38 (s, 3H, MeO), 4.56 (s, 1H, HCO). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 38.86 (Me_2N), 55.62 (MeO), 86.89 (CH), 113.92 (CN).

6: ^1H NMR ($CDCl_3$) δ: 3.97 (s, 3H, MeO), 4.00 (s, 3H, MeO), 4.26 (s, 3H, MeN).

7: yield 93%, mp 69–70 °C. ^1H NMR ($CDCl_3$) δ: 1.7, 1.73 (tt, 4H, CCH_2CH_2C), 2.79, 2.82 (t, 4H, CH_2NCH_2), 3.97 (s, 6H, 2MeO), 5.51 (s, 2HNCH_2N).

8: yield 87%, mp 180–181 °C. ^1H NMR ($CDCl_3$) δ: 2.71 [s, 8H, $N(CH_2CH_2)_2N$], 3.98 (s, 12H, 4MeO), 5.30 (s, 4H, $2NCH_2N$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 48.86 [$N(CH_2CH_2)_2N$], 52.49 (4MeO), 72.68 ($2NCH_2N$), 139.74 (C=N), 160.21 (C=O).

9: ^1H NMR ($CDCl_3$) δ: 3.31 [s, 8H, $N(CH_2CH_2)_2N$], 3.96 (s, 6H, 2MeO), 3.97 (s, 6H, 2MeO), 4.44 (s, 4H, $2NCH_2N$).

10: yield 61%, mp 127–128 °C. ^1H NMR ($CDCl_3$) δ: 3.96 (s, 12H, 4MeO), 4.26 (s, 2H, PhCH_2N), 5.62 (s, 4H, $2NCH_2N$), 7.1 (m, 5H, Ph), $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ: 52.28 (4MeO), 54.39 (PhCH_2N), 72.44 ($2NCH_2N$), 127.66, 128.28, 128.54, 135.25 (Ph), 139.54 (C=N), 159.71 (C=O).

3 (*a*) H. Böhme and D. Morf, *Chem. Ber.*, 1958, **91**, 660; (*b*) M. B. Frankel and D. O. Woolery, *J. Org. Chem.*, 1983, **48**, 611; (*c*) T. B. Brill, R. J. Karpowicz, T. M. Haller and A. L. Rheingold, *J. Phys. Chem*., 1984, **88**, 4138; (*d*) Y. Oyumi, A. L. Rheingold and T. B. Brill, *J. Phys. Chem*., 1987, **91**, 920; (*e*) A. Hassner, M. Stern, H. E. Cottlieb and F. Frolow, *J. Org. Chem.*, 1990, **55**, 2304; (*f*) P. Magnus, T. Lacour and W. Weber. *J. Am. Chem. Soc*., 1993, **115**, 9347; (*g*) M. N. S. Rad, S. Behrouz and A. Khalafi-Nezhad, *Tetrahedron Lett*., 2007, **48**, 3445.

4 G. K. Surya Prakash, H. Vaghoo, Ch. Panja, V. Surampudi, R. Kultyshev and T. Mathew, *Proc. Natl. Acad. Sci. USA*, 2007, **104**, 3026.

5 (*a*) O. G. Nabiev, M. A. Shachgeldiev, I. I. Chervin and R. G. Kostyanovsky, *Dokl. Akad. Nauk SSSR*, 1985, **284**, 872 (in Russian); (*b*) A. V. Bogatsky, N. G. Lukyanenko, V. N. Pastushok and R. G. Kostyanovsky, *Synthesis*, 1983, **12**, 992; (*c*) A. V. Bogatsky, N. G. Lukyanenko, V. N. Pastushok and R. G. Kostyanovsky, *Dokl. Akad. Nauk SSSR*, 1982, **265**, 619 (in Russian); (*d*) R. G. Kostyanovskii, A. E. Polyakov, M. D. Isabaev, G. K. Kadorkina and V. I. Markov, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1974, 1444 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1974, **23**, 1373); (*e*) R. G. Kostyanovskii and O. A. Pan'shin, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1965, 740 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1965, **14**, 721); (*f*) R. G. Kostyanovskii and O. A. Pan'shin, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*., 1963, 182 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1963, **12**, 164).

Received: 30th March 2009; Com. 09/3310