ISSN 1070-3632, Russian Journal of General Chemistry, 2017, Vol. 87, No. 12, pp. 2887–2890. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © M.F. Pistsov, O.M. Lavrova, A.M. Saifutdinov, R.N. Burangulova, L.M. Kustov, F.I. Guseinov, R.Z. Musin, 2017, published in Zhurnal Obshchei Khimii, 2017, Vol. 87, No. 12, pp. 2076–2079.

LETTERS TO THE EDITOR

Dedicated to B.I. Buzykin on the 80th Anniversary of His Birth

Synthesis of Functionally Substituted Cyano Carbonyl Compounds

M. F. Pistsov[a,b]*, O. M. Lavrova[a], A. M. Saifutdinov[a,b], R. N. Burangulova[a], L. M. Kustov[c], F. I. Guseinov[a,c], and R. Z. Musin[a,d]

[a] *Kazan National Research Technological University, ul. K. Marksa 68, Kazan, 420015 Tatarstan, Russia*
**e-mail: mihail.p.f@mail.ru*
[b] *Immanuel Kant Baltic Federal University, ul. A. Nevskogo 14, Kaliningrad, 236016 Russia*
[c] *Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii pr. 47, Moscow, 119991 Russia*
[d] *Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center, Russian Academy of Sciences, ul. Arbuzova 8, Kazan, 420088 Tatarstan, Russia*

Received July 31, 2017

Abstract—Functionally substituted cyano carbonyl compounds have been synthesized by reactions of 1-chloro-oxiranecarbaldehyde acetals and α-chlorobenzyl diethoxymethyl ketones with potassium cyanide in DMF.

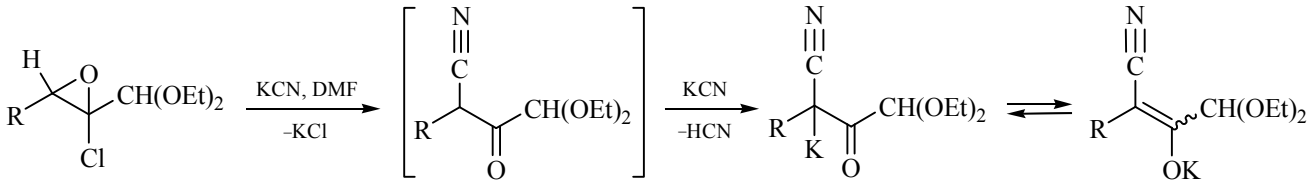
Keywords: chlorooxiranes, chloro ketones, potassium salts, potassium cyanide, cyanooxiranes
DOI: 10.1134/S1070363217120234

Chlorooxiranes containinf an acetal moiety are promising starting compounds for the synthesis of various heterocyclic systems, in particular heterocyclic aldehydes and their derivatives. Our previous studies have shown that chlorooxiranes **1** and isomeric chloro ketones **2** react with O-, S-, P-, and N-mono- and polynucleophiles to give various heterocycles via formation of a new C–C bond and redox processes leading to α-hydroxy acids [1–10].

It is known that reactions of halocarbonyl compounds with cyanide ion take two main pathways. One pathway involves attack of cyanide ion on the carbonyl carbon atom with formation of cyanooxiranes or Favorskii rearrangement leads to cyanocyclopropanols. The other pathway is nucleophilic substitution of halogen by cyano group [11–16].

In order to extent the synthetic potential of chlorooxiranes, we studied reactions of electrophiles **1** and **2** with potassium cyanide. The reactions were carried out in DMF at room temperature (5–6 h), and the products were potassium salts **4** (**5**) resulting from opening of the oxirane ring (Scheme 1). We failed to isolate the primary products, α-cyano ketones **3**, since they, being strong CH acids, reacted with the second KCN molecule to form the corresponding potassium salts capable of existing as both keto (**4**) and enolate isomers (**5**).

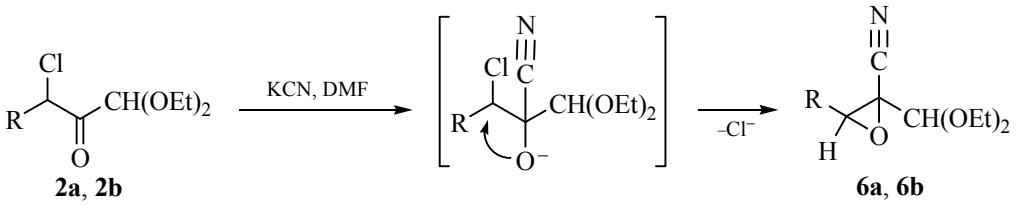
Scheme 1.



1a–**1c** **3** **4a**–**4c** **5a**–**5c**

R = Ph (**a**), *p*-Cl-Ph (**b**), Me (**c**).

Scheme 2.



2a, **2b** **6a**, **6b**

R = Ph (**a**), *p*-Cl-Ph (**b**).

The product structure was proved by ^{1}H and ^{13}C NMR and MALDI mass spectra. The ^{1}H NMR spectra of **5** showed that both aromatic and acetal moieties were conserved in their molecules. Signals in the region δ ~6.9–8.1 ppm were assigned to aromatic protons, and the acetal proton signal was a singlet at δ 5.4 ppm.

The enolate structure of **5** followed from the ^{13}C NMR data. The α-carbon nucleus in enols resonates at δ_C 140–160 ppm, and the β-carbon nucleus, at δ_C ~80–100 ppm [17, 18]. The chemical shift of the double-bonded carbon atom linked to the cyano group in acrylonitriles is about 140 ppm, and the signal of the other double-bonded carbon atom appears at δ_C 115 ppm or more upfield [19, 20]. Taking into account that the β-carbon atom of the enol fragment of **5** is directly linked to the cyano group, the chemical shifts of the double-bonded carbon atoms are well consistent with published data. Therefore, the signal at δ_C 72–73 ppm can be assigned with a high degree of certainty to the β-carbon atom, and the signal at δ_C ~179–180 ppm, to the α-carbon atom. The signal at δ_C 120–123 ppm belongs to the cyano group, since the range of chemical shifts of the cyano carbon atoms in acrylonitriles [19, 20] and some enol derivatives [17] is δ_C ~115–120 ppm. Carbon atoms of the aromatic ring gave signals at δ_C ~140 and 127–123 ppm [17, 18]. The signals at δ_C ~15 and ~62 ppm belong to the methyl and methylene groups, respectively, and the acetal carbon atom has a chemical shift of δ_C ~100 ppm.

The mass spectrum of **5a** showed a strong peak of the protonated molecular ion $[M + H]^+$ with *m*/*z* 286. The ion with *m*/*z* 324 is heavier by 38 a.m.u., which corresponds to addition of potassium ion to the initial molecule to give $[M + K]^+$. A different fragmentation pattern was observed for compound **5b**. In this case, the most intense and informative were peaks with *m*/*z* 318 and 284. The first of these corresponds to elimination of hydrogen ($[M – H]^+$), and the second, to loss of chlorine from the molecular ion ($[M – Cl]^+$).

α-Chloro ketones **2** reacted with potassium cyanide in DMF at room temperature to give cyanooxiranes **6** in high yield (Scheme 2). The ^{1}H NMR spectra of compounds **6** contained signals of the CH proton in the oxirane ring (δ 4.49–4.51 ppm), acetal proton (δ 4.84–4.86 ppm), and protons of the aromatic ring (δ 7.52–7.78 ppm). In the ^{13}C NMR spectrum of **6**, the cyano carbon atom resonated at δ_C 115 ppm, and no carbonyl carbon signal was observed.

Potassium 1-cyano-3,3-diethoxy-1-phenylprop-1-en-2-olate (5a). Chlorooxirane **1a**, 1 g (3.90 mmol), was added with stirring to a suspension of 0.506 g (7.80 mmol) of potassium cyanide in 10 mL of DMF. The mixture was stirred for 5 h at room temperature and was then heated for 1 h at 80°C. The solvent was removed under reduced pressure, the residue was treated with 10 mL of ethanol, the precipitate was filtered off, and the filtrate was evaporated. The white crystalline solid was filtered off, washed with diethyl ether (2–10 mL), and dried under reduced pressure. Yield 0.62 g (65%), mp 150–153°C. IR spectrum, ν, cm^{-1}: 1055 s (C–O–C), 1537 s (C=C$_{arom}$), 2170 s (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.21 t (6H, $OCH_2C\underline{H}_3$, J = 6.6 Hz), 3.59–3.81 m (4H, $OC\underline{H}_2CH_3$), 5.50 s [1H, C$\underline{H}$(OEt)$_2$], 6.80 t (1H, *p*-H, $^3J_{HH}$ = 7.2 Hz), 7.11 t (2H, *m*-H, $^3J_{HH}$ = 7.2 Hz), 8.11 d (2H, *o*-H, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 15.71 ($OCH_2\underline{C}H_3$), 62.11 ($O\underline{C}H_2CH_3$), 73.19 (NC$\underline{C}$=C), 100.61 [$\underline{C}$H(OEt)$_2$], 121.08 (C≡N), 123.64 (C^p), 127.65 (C^o), 127.72 (C^m), 140.13 (C^i), 179.34 (C=$\underline{C}$OK). Mass spectrum (MALDI), *m*/*z* (I_{rel}, %): 286 (100) $[M + H]^+$, 324 (30) $[M + K]^+$. Found, %: C 58.83; H 5.56; N 4.82. $C_{14}H_{16}KNO_3$. Calculated, %: C 58.92; H 5.65; N 4.91.

Potassium 1-(4-chlorophenyl)-1-cyano-3,3-diethoxyprop-1-en-2-olate (5b) was synthesized in a similar way from 1 g (3.436 mmol) of chlorooxirane **1b** and 0.446 g (6.872 mmol) of KCN. Yield 0.7 g (64%), mp 210–213°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.22 t (6H, $OCH_2C\underline{H}_3$, J = 7.2 Hz), 3.19–3.58 m

(4H, OC<u>H</u>$_2$CH$_3$), 5.42 s [1H, C<u>H</u>(OEt)$_2$], 7.09 (2H, *m*-H, $^3J_{HH}$ = 8.4 Hz), 8.11 d (2H, *o*-H, $^3J_{HH}$ = 8.4 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 15.79 (OCH$_2$<u>C</u>H$_3$), 61.78 (O<u>C</u>H$_2$CH$_3$), 72.77 (NC<u>C</u>=C), 100.35 [<u>C</u>H(OEt)$_2$], 123.88 (C≡N), 124.56 (C^p), 127.44 (C^o), 127.48 (C^m), 139.66 (C^i), 180.08 (C=<u>C</u>OK). Mass spectrum (MALDI), *m*/*z* (I_{rel}, %): 318 (100) [*M* – H]$^+$, 284 (45) [*M* – Cl]$^+$. Found, %: C 52.67; H 4.81; Cl 11.14; N 4.51. $C_{14}H_{15}ClKNO_3$. Calculated, %: C 52.58; H 4.73; Cl 11.09; N 4.38.

Potassium 3-cyano-1,1,-diethoxybut-2-en-2-olate (5c) was synthesized in a similar way from 1 g (5.137 mmol) of chlorooxirane **1c** and 0.667 g (10.274 mmol) of KCN. Yield 0.73 g (64%), mp 173–175°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.10 t (6H, OCH$_2$C<u>H</u>$_3$, *J* = 7.0 Hz), 1.47 s (3H, CH$_3$), 3.34–3.67 m (4H, OC<u>H</u>$_2$CH$_3$), 4.99 s [1H, C<u>H</u>(OEt)$_2$]. ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 15.79 (OCH$_2$<u>C</u>H$_3$), 26.25 (<u>C</u>H$_3$C=C), 61.78 (O<u>C</u>H$_2$CH$_3$), 72.77 (NC<u>C</u>=C), 100.35 [<u>C</u>H(OEt)$_2$], 123.34 (C≡N), 180.07 (C=<u>C</u>OK). Found, %: C 48.52; H 6.43; N 6.38. $C_9H_{14}KNO_3$. Calculated, %: C 48.41; H 6.32; N 6.27.

2-(Diethoxymethyl)-3-phenyloxirane-2-carbonitrile (6a) was synthesized in a similar way from 5 g (19.53 mmol) of chloro ketone **2a** and 2.60 g (40 mmol) of KCN. The product was isolated by vacuum distillation. Yield 3.91 g (81%), bp 132–134°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.31–1.50 m (6H, OCH$_2$C<u>H</u>$_3$), 3.78–3.93 m (4H, OC<u>H</u>$_2$CH$_3$), 4.49 s (1H, 3-H), 4.84 s [1H, C<u>H</u>(OEt)$_2$], 7.52 s (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 15.12 (OCH$_2$<u>C</u>H$_3$), 58.10 (C^2), 59.76 (O<u>C</u>H$_2$CH$_3$), 64.38 (C^3), 99.39 [<u>C</u>H(OEt)$_2$], 115.12 (C≡N), 126.43 (C^o), 128.58 (C^p), 129.55 (C^m), 131.49 (C^i). Found, %: C 68.15; H 7.06; N 5.78. $C_{14}H_{17}NO_3$. Calculated, %: C 68.00; H 6.93; N 5.66.

3-(4-Chlorophenyl)-2-(diethoxymethyl)oxirane-2-carbonitrile (6b) was synthesized in a similar way from 5 g (17.18 mmol) of chlorooxirane **2b** and 2.60 g (40 mmol) of KCN. The product was isolated by vacuum distillation. Yield 3.81 g (79%), bp 142–144°C (0.05 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.29–1.48 m (6H, OCH$_2$C<u>H</u>$_3$), 3.76–3.91 m (4H, OC<u>H</u>$_2$CH$_3$), 4.51 s (1H, 3-H), 4.86 s [1H, C<u>H</u>(OEt)$_2$], 7.78 s (4H, C$_6$H$_4$). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.92 (OCH$_2$<u>C</u>H$_3$), 58.17 (C^2), 59.65 (O<u>C</u>H$_2$CH$_3$), 62.81 (C^3), 100.02 [<u>C</u>H(OEt)$_2$], 115.14 (C≡N), 126.21 (C^o), 128.26 (C^p), 129.16 (C^m), 132.76 (C^i). Found, %: C 59.80; H 5.83; Cl 12.62; N 5.08. $C_{14}H_{16}ClNO_3$. Calculated, %: C 59.68; H 5.72; Cl 12.58; N 4.97.

The IR spectra were recorded in the range from 400 to 4000 cm^{-1} on a Bruker Vektor 22 spectrometer with Fourier transform. The ^{1}H NMR spectra were recorded on a Tesla BW 567 spectrometer (100 MHz). The ^{13}C NMR spectra were measured on a Bruker AM-300 instrument (300 MHz). The mass spectra (MALDI) were obtained on a Bruker Ultraflex III instrument (Germany) equipped with a solid state laser and time-of-flight mass analyzer. The purity of the isolated compounds was checked by TLC on ALUGRAM SIL G/UV$_{254}$; spots were visualized by treatment with iodine vapor and under UV light (λ 254, 365 nm).

ACKNOWLEDGMENTS

This study was performed under financial support by the Russian Science Foundation (project no. 14-50-00126) and also by of the 5-100 project for increasing the rating of leading Russian universities among world's scientific educational centers.

REFERENCES

1. Guseinov, F.I., Pistsov, M.F., Lavrova, O.M., Burangulova, R.N., and Garifullin, M.R., *Vestn. Kazan. Tekhnol. Univ*., 2012, vol. 15, no. 14, p. 35.
2. Lavrova, O.M., Pistsov, M.F., Valiullina, R.Zh., Guseinov, F.I., and Burangulova, R.N., *Vestn. Kazan. Tekhnol. Univ*., 2011, vol. 14, no. 11, p. 108.
3. Pavlov, V.A., Kurdyukov, A.I., Plemenkov, V.V., Khaliullin, R.R., and Moskva, V.V., *Russ. J. Gen. Chem*., 1993, vol. 63, no. 3, p. 449.
4. Guseinov, F.I. and Moskva, V.V., *Russ. J. Org. Chem*., 1994, vol. 30, no. 3, p. 384.
5. Guseinov, F.I., Tagiev, S.Sh., and Moskva, V.V., *Russ. J. Org. Chem*., 1995, vol. 31, no. 1, p. 86.
6. Guseinov, F.I., Tagiev, S.Sh., and Moskva, V.V., *Russ. J. Org. Chem*., 1995, vol. 31, no. 8, p. 1028.
7. Guseinov, F.I., Burangulova, R.N., and Moskva, V.V., *Russ. J. Gen. Chem*., 1997, vol. 67, no. 1, p. 157.
8. Guseinov, F.I., Yudina, N.A., and Klimentova, G.Yu., *Chem. Heterocycl. Compd*., 1998, vol. 34, no. 2, p. 167. doi 10.1007/BF02315178
9. Guseinov, F.I., Burangulova, R.N., Mukhamedzyanova, E.F., Strunin, B.P., Sinyashin, O.G., Litvinov, I.A., and Gubaidullin, A.T., *Chem. Heterocycl. Compd*., 2006, vol. 42, no. 7, p. 943. doi 10.1007/s10593-006-0184-1
10. Asadov, Kh.A., Guseinov, F.I., Strunin, B.P., Beskrovnyi, D.V., and Litvinov, I.A., *Chem. Heterocycl. Compd*., 2006, vol. 42, no. 8, p. 1059. doi 10.1007/s10593-006-0204-1

11. Abad, A., Agullu, C., Arno, M., and Seoane, E., *Tetrahedron*, 1986, vol. 42, p. 2429. doi 10.1016/0040-4020(86)80006-0
12. Takahashi, K., Nishizuka, T., and Iida, H., *Synth. Commun*., 1981, vol. 11, p. 757. doi 10.1080/00397918108063654
13. Saito, K. and Harada, K., *Tetrahedron Lett*., 1989, vol. 30, p. 1651. doi 10.1016/S0040-4039(00)99544-3
14. Gallons, H., Girardeau, J.F., and Combet-Farnoux, C., *Bull. Soc. Chim. Fr*., 1977, vol. 44, p. 936.
15. Burdukov, A.B., Roschupkina, G.I., Gatilov, Y.V., Gromilov, S.A., and Reznikov, V.A., *J. Supramol. Chem*., 2002, vol. 2, p. 359. doi 10.1016/S1472-7862(03)00059-5
16. Buttke, K. and Niclas, H.J., *Synth. Commun*., 1994, vol. 24, p. 3241. doi 10.1080/00397919408010246
17. *The Chemistry of Enols*, Rappoport, Z., Ed., Chichester: Wiley, 1990, p. 152.
18. Frey, J., Eventova, I., Rappoport, Z., Müller, T., Takai, Y., and Sawada, M., *J. Chem. Soc., Perkin Trans. 2*, 1995, p. 621. doi 10.1039/P29950000621
19. Barfield, M., Gotoh, T., and Hall, H.K., *Magn. Reson. Chem*., 1985, vol. 23, p. 705. doi 10.1002/mrc.1260230905
20. Asiri, A.M., Karabacak, M., Kurt, M., and Alamry, K.A., *Spectrochim. Acta, Part A*, 2011, vol. 82, p. 444. doi 10.1016/j.saa.2011. 07.076