Nitrilation of Carboxylic Acids with Acetonitrile Catalyzed by Molybdenum and Vanadium Complexes

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Abstract—Various carbonitriles were synthesized by reaction of the corresponding carboxylic acids with acetonitrile in carbon tetrachloride in the presence of $VO(acac)_2$ and $Mo(CO)_6$ in 6 h at 150–170°C.

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Nitriles constitute a very important class of organic compounds. They are used as solvents and intermediate products for the synthesis of drugs, pesticides, and plasticizers. The most important compounds of the nitrile series are acetonitrile (universal solvent), acrylonitrile (monomer for synthetic fiber), and adiponitrile (starting compound for the synthesis of caprolactam and hexamethylenediamine). The use of acetonitrile and benzonitrile as promoters of manganese catalysts for the oxidation of toluene increases the conversion of toluene by a factor of 15 and reduces the catalyst consumption by a factor of 28. Benzonitrile is a starting material for the manufacture of formaldehyde resins, azeotropic agent for the separation of naphthalene-alkylnaphthalene mixtures, and solvent for chlorinated rubber and cellulose nitrates and acetates [1, 2].

Classical methods for the preparation of nitriles are based on addition of hydrogen cyanide to olefins and 1,3-dienes, oxidative ammonolysis (400–500°C), dehydration of carboxylic acid amides and ammonium salts, radical cyanation of alkyl iodides, oxidation of



amines in the presence of NiO₂ at $300-350^{\circ}$ C, and graphite- or sodium iodide-catalyzed cyanation of aldehydes with hydroxylamine hydrochloride [3–7].

Aliphatic C_7 – C_{17} nitriles were synthesized in 50– 57% yield by reaction of acetonitrile with the corresponding aliphatic carboxylic acids at 270°C [8]; for this purpose, 10-fold excess of sulfuric acid was used as catalyst [9]. Apart from nitriles, the reaction mixtures contained the corresponding amide and *N*-acetyl amide at a ratio of 3:1:3.

Reactions of carboxylic acids with acetonitrile can be catalyzed by transition metal complexes such as $Fe(acac)_3$, $Co(acac)_3$, $Cu(acac)_2$, $Pd(acac)_2$, $Mo(CO)_6$, $Rh(acac)_3$, and $VO(acac)_2$. Table contains the results of the reaction of benzoic acid as model substrate with acetonitrile in the presence of different metal complexes (Scheme 1). It is seen that the best catalysts are $VO(acac)_2$ and $Mo(CO)_6$. The reaction of benzoic acid

Reaction of benzoic acid with acetonitrile in the presence of different catalysts

Catalyst	Temperature, °C	Time, h	Yield of benzonitrile, %
Fe(acac) ₃	200	3	30
$Co(acac)_3$	200	3	63
$Cu(acac)_2$	200	3	65
$Pd(acac)_2$	200	3	85
$Rh(acac)_3$	200	3	94
$VO(acac)_2$	170	3	100
$Mo(CO)_6$	150	6	100



(1a) with acetonitrile in the presence of $Mo(CO)_6$ at a [Mo]–1a–MeCN–CCl₄ molar ratio of 1:100:(300– 500):(50–300) was complete in 6 h at 150°C, and benzonitrile (1b) was formed in quantitative yield. In all cases, excess acetonitrile was used since it was simultaneously the reagent and the solvent. A necessary condition for successful nitrilation was the presence of carbon tetrachloride as co-solvent. Further experiments were carried out with $Mo(CO)_6$ and $VO(acac)_2$ as catalysts.

In the series of substituted benzoic acids, the yields of the corresponding nitriles depended on the nature of substituents and their position. The effect of the *para* substituent on the reaction course was insignificant. The reactions of acetonitrile with 4-methylbenzoic, 4-methoxybenzoic, 4-bromobenzoic, and 4-chlorobenzoic acids 2a-5a smoothly afforded substituted benzonitriles 2b (92%), 3b (88%), 4b (72%), and 5b(73%) (Scheme 2). Unexpectedly, the reaction of acetonitrile with salicylic acid (6a) in the presence of VO(acac)₂ led to the formation of 2-chlorobenzonitrile (6b) due to concurrent replacement of the hydroxy group by chlorine with participation of carbon tetrachloride. 3-Hydroxybenzoic acid (7a) reacted with acetonitrile in a similar way (Scheme 3).

2-Chlorobenzonitrile (**6b**) was also obtained in 70% yield from 2-chlorobenzoic acid (**8a**) and acetonitrile in the presence of VO($(acac)_2$, whereas the yield of **6b**

in the reaction catalyzed by $Mo(CO)_6$ was as low as 28%. Methyl 2-methoxybenzoate (9a) was converted into 2-methoxybenzonitrile (9b, yield 66%) in the presence of $Mo(CO)_6$ (Scheme 4).

1- and 2-Naphthoic acids **10a** and **11a** reacted with acetonitrile in the presence of $Mo(CO)_6$ at a higher temperature (170°C) to form naphthalene-1-carbonitrile (**10b**) and naphthalene-2-carbonitrile (**11b**) in 77% and 82% yield, respectively (Scheme 5). The yields of **10b** and **11b** at 150°C did not exceed 40–50%.

Adamantane-1-carboxylic acid (12a) vigorously reacted with acetonitrile in the presence of $Mo(CO)_6$ to give a mixture of adamantane-1-carbonitrile (12b) and 3-chloroadamantane-1-carbonitrile (12c) at a ratio of 2:1 with a quantitative overall yield. When $VO(acac)_2$ was taken as catalyst, nitrile 12b was formed as the only product (Scheme 6). Aliphatic carboxylic acids, specifically propionic (13a), butyric (14a), valeric (15a), and decanoic (16a) showed high reactivity toward acetonitrile under catalysis by $Mo(CO)_6$ and VO(acac)₂. Regardless of the carbon chain length, the corresponding nitriles (13b-16b) were obtained with high yields (Scheme 7). The reactivity of dicarboxylic acids depended on the length of the carbon chain connecting the carboxy groups. Malonic acid failed to react with acetonitrile, whereas the reaction of adipic acid (17a) with acetonitrile under catalysis by $VO(acac)_2$ smoothly afforded adiponitrile (17b)





/O(acac)₂, 150°C, 6 h

Scheme 7.

12h





(Scheme 8). The reaction of terephthalic acid (**18a**) with MeCN in the presence of $VO(acac)_2$ in CCl₄ was very vigorous, while no reaction was observed with phthalic or isophthalic acid.

18a

12a

The yields of nitriles decreased as the reaction time increased, presumably due to reversibility of the reaction. The yields refer to the isolated product. The product structure was determined by spectral methods and by comparison with authentic samples.

EXPERIMENTAL

The ¹³C NMR spectra were recorded on a Bruker Avance-400 spectrometer (100.62 MHz) using CDCl₃ as solvent. The mass spectra were obtained on a Shimadzu GCMS-QP2010Plus instrument (SPB-5 capillary column, 30 m×0.25 mm; carrier gas helium; oven temperature programming from 40 to 300°C at a rate of 8 deg/min; injector temperature 280°C, ion source temperature 200°C; electron impact, 70 eV). The elemental compositions were determined with a Carlo Erba 1106 analyzer.

18b

The reactions were carried in sealed ampules or in a stainless steel high-pressure microreactor. The progress of reactions and the purity of the isolated compounds were monitored by GLC on Shimadzu GC-9A and GC-2014 instruments (2 m×3-mm column packed with 5% of SE-30 on Chromaton N-AW-HMDS; oven temperature programming from 50 to 270°C at 8 deg/min; carrier gas helium, flow rate 47 mL/min). General procedure for the reaction of acetonitrile with carboxylic acids. A 17-mL stainless-steel high-pressure microreactor was charged with 1 mmol of Mo(CO)₆ or VO(acac)₂, 100 mmol of carboxylic acid, 500 mmol of acetonitrile, and 50 mmol of carbon tetrachloride. The reactor was hermetically closed and heated for 6 h at 150°C. When the reaction was complete, the reactor was cooled to room temperature and opened, the mixture was filtered through a layer of Al_2O_3 , unreacted acetonitrile and carbon tetrachloride were distilled off, and the residue was distilled under atmospheric or reduced pressure or recrystallized from ethanol.

Benzonitrile (1b). Yield 98%, bp 95–96°C (30 mm); published data [10]: bp 191°C. ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 111.77 (C¹), 118.30 (CN), 128.65 (C³, C⁵), 131.52 (C², C⁶), 132.30 (C⁴). Mass spectrum, *m/z* (*I*_{rel}, %): 103 (100) [*M*]⁺, 104 (7.4), 77 (5.6), 76 (32.5), 75 (7.5), 59 (4), 52 (5.7), 50 (17.2), 43 (12), 39 (6.7), 37 (4.6), 39 (6.7).

4-Methylbenzonitrile (2b). Yield 92%, mp 37– 37.5°C (from EtOH); published data [10]: mp 38°C. ¹³C NMR spectrum, δ_C , ppm: 21.74 (CH₃), 109.27 (C¹), 119.30 (CN), 129.65 (C³, C⁵), 132.02 (C², C⁶), 143.68 (C⁴). Found, %: C 82.15; H 6.48; N 11.28. C₈H₇N. Calculated, %: C 82.02; H 6.02; N 11.96.

4-Methoxybenzonitrile (3b). Yield 88%, mp 62–63°C (from MeOH); published data [10]: mp 62°C. ¹³C NMR spectrum, δ_C , ppm: 55.55 (OCH₃), 104.03 (C¹), 114.72 (C³, C⁵), 119.15 (CN), 134.12 (C², C⁶), 162.88 (C⁴).

4-Bromobenzonitrile (4b). Yield 70%, mp 111– 111.5°C (from hexane–MeOH); published data [10]: mp 112°C. ¹³C NMR spectrum, δ_C , ppm: 111.19 (C¹), 117.90 (CN), 127.76 (C⁴), 132.68 (C³, C⁵), 133.27 (C², C⁶).

4-Chlorobenzonitrile (5b). Yield 73%, mp 90– 91°C (from EtOH); published data [10]: mp 92°C. ¹³C NMR spectrum, δ_C , ppm: 110.79 (C¹), 117.90 (CN), 129.68 (C³, C⁵), 133.27 (C², C⁶), 139.87 (C⁴).

2-Chlorobenzonitrile (6b). Yield 75%, mp 42.5–43°C (from EtOH); published data [10]: mp 43°C. ¹³C NMR spectrum, δ_{C} , ppm: 113.42 (C¹), 116.98 (CN), 127.35 (C⁵), 128.99 (C³), 133.12 (C⁶), 134.71 (C²), 135. 88 (C⁴).

3-Chlorobenzonitrile (7b). Yield 72%, mp 41–42°C (from hexane–MeOH); published data [10]: mp 41°C [10]. ¹³C NMR spectrum, δ_C , ppm: 113.42

(CN), 113.87 (C¹), 129.99 (C⁶), 130.36 (C⁵), 131.84 (C²), 133.17 (C⁴), 135.12 (C³).

2-Methoxybenzonitrile (9b). Yield 66%, bp 98.7°C (3 mm). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 109.04 (C¹), 112.95 (C³), 117.52 (CN), 121.34 (C⁵), 133.96 (C⁶), 135.82 (C⁴), 161.38 (C²). Mass spectrum, *m/z* (*I*_{rel}, %): 133 (100) [*M*]⁺, 134 (7), 132 (29), 104 (12), 103 (19), 102 (5), 90 (31), 78 (7), 77 (5), 76 (10), 75 (7), 64 (12), 63 (14), 50 (5), 39 (12).

Naphthalene-1-carbonitrile (10b). Yield 77%, mp 35.5–36°C (from EtOH); published data [10]: mp 35°C. ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 110.11 (C¹), 118.12 (CN), 125.23 (C³), 127.37 (C⁷), 127.80 (C^{8a}), 128.96 (C⁸), 129.44 (C⁶), 131.76 (C²), 132.43 (C^{4a}), 132.87 (C⁵), 133.42 (C⁴).

Naphthalene-2-carbonitrile (11b). Yield 82%, mp 66–67°C (from EtOH); published data: mp 66°C. ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 109.45 (C²), 119.22 (CN), 126.37 (C³), 127.75 (C⁸), 128.06 (C⁶), 128.44 (C^{8a}), 129.06 (C⁷), 129.20 (C⁴), 132.27 (C^{4a}), 134.06 (C¹), 134.65 (C⁵).

Adamantane-1-carbonitrile (12b). Yield 98%, mp 193.5–194°C (from MeOH); published data [11]: mp 193–194°C. Mass spectrum, m/z (I_{rel} , %): 161 (57) $[M]^+$, 162 (7), 160 (12), 146 (21), 135 12), 134 (100), 133 (5), 132 (5), 120 (5), 119 (10), 118 (7), 107 (7), 106 (7), 105 (15), 104 (14), 95 (19), 94 (21), 93 (48), 92 (10), 91 (14), 81 (4), 80 (4), 79 (19), 78 (7), 77 (14), 69 (19), 68 (7), 67 (10), 66 (5), 65 (7), 55 (7), 54 (7), 53 (7), 51 (5), 41 (19), 39 (19).

3-Chloroadamantane-1-carbonitrile (12c). Yield 32%, mp 208–209°C (from MeOH); published data [12]: mp 208.5–209°C. Mass spectrum, m/z (I_{rel} , %): 195 (12) [M]⁺, 168 (7.1), 161 (12), 160 (100), 159 (7), 128 (6.5), 118 (10), 105 (6.3), 104 (14), 93 (13.4), 92 (10), 91 (13), 79 (10), 77 (13), 65 (11), 55 (6), 53 (8), 41 (21.5), 39 (25).

Propanenitrile (13b). Yield 82%, bp 96–97°C; published data [10]: bp 97°C. Mass spectrum, m/z $(I_{rel}, \%)$: 55 (10) $[M]^+$, 54 (62.2), 53 (7.1), 52 (11), 51 (8.7), 28 (100), 27 (18.4), 26 (20.5), 23 (7.5), 15 (8.6).

Butanenitrile (14b). Yield 80%, bp 118–119°C; published data [10]: bp 118°C. Mass spectrum, *m/z* (*I*_{rel}, %): 42 (4.3), 41 (100), 40 (4), 39 (9.2), 38 (4), 29 (62.4), 28 (10), 27 (33.6), 26 (7.5), 15 (4.1).

Pentanenitrile (15b). Yield 78%, bp 75°C (70 mm); published data [10]: bp 141°C. ¹³C NMR spectrum, δ_C , ppm: 13.18 (C⁵), 16.92 (C²), 21.87 (C⁴), 27.41 (C³), 119.84 (CN).

RUSSIAN JOURNAL OF ORGANIC CHEMISTRY Vol. 52 No. 9 2016

Decanenitrile (16b). Yield 70%, bp 97–98°C (5 mm); published data [10]: bp 245°C. ¹³C NMR spectrum, δ_{C} , ppm: 14.08 (C¹), 22.69 (C⁹), 24.99 (C³), 28.82 (C⁴), 29.12 (C⁶, C⁷), 29.33 (C⁵), 31.97 (C⁸), 119.82 (CN).

Hexanedinitrile (17b). Yield 72%, bp 129–130°C (3 mm); published data [10]: bp 295°C. ¹³C NMR spectrum, δ_C , ppm: 16.45 (C², C⁵), 24.28 (C³, C⁴), 119.29 (CN).

Benzene-1,4-dicarbonitrile (18b). Yield 80%, mp 226.5–227°C (from EtOH); published data [10]: mp 224–227°C. ¹³C NMR spectrum, δ_{C} , ppm: 115.97 (C¹, C⁴), 117.65 (CN), 131.62 (C², C³, C⁵, C⁶).

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