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SHORT COMMUNICATIONS

Bicyclic *ortho*-Aminocarbonitriles—New Accessible Synthons

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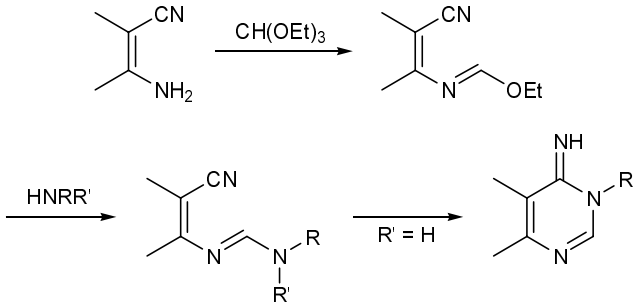
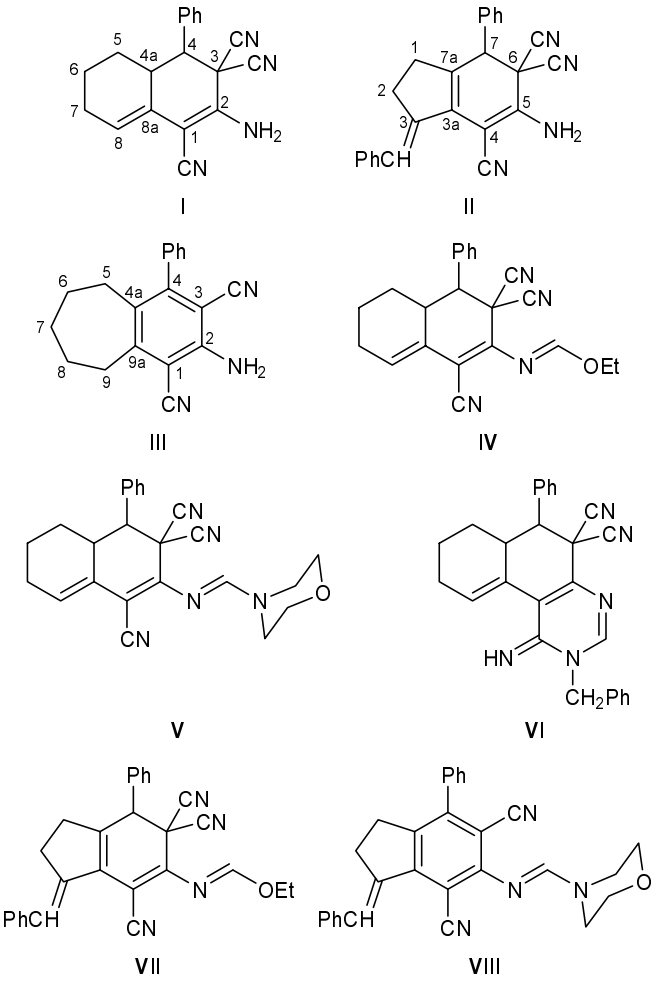
ortho-Aminocarbonitriles are widely used in organic synthesis for the preparation of various heterocyclic compounds [1]. One of the research lines developed in our laboratory includes reactions of *ortho*-aminocarbonitriles with triethyl orthoformate which lead to formation of reactive imidic acid esters; the latter readily exchange the ethoxy group for amino [2, 3]. The reactions with secondary amines stop at the stage of amidine formation, while primary amines give rise to subsequent pyrimidine ring closure (Scheme 1).

Scheme 1.



While continuing these studies, we focused on a novel compound of the *ortho*-aminocarbonitrile series, 2-amino-4-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-1,3,3-tricarbonitrile (**I**), which was recently synthesized by A.M. Shestopalov and co-workers [4] by base-catalyzed reaction of benzylidenemalononitrile with cyclohexanone. With the goal of extending the series of these interesting compounds, we performed reactions of benzylidenemalononitrile with cyclopentanone and cycloheptanone under analogous conditions. It turned out that, depending on the ring size in the initial cycloalkanone, different products were formed: compound **II** from cyclopentanone and compound **III** from cycloheptanone.

Some synthetic potentialities of synthons **I**–**III** are illustrated by Scheme 1. Following this scheme, we obtained new compounds **IV**–**VIII**. The reaction of formimidic acid ester **VII** with morpholine was accompanied by aromatization of the six-membered carbocycle, while the imidic ester fragment did not change in an analogous reaction with compound **IV**.



The structure of all newly synthesized compounds was confirmed by their analytical and spectral data. Signals in the ^{1}H NMR spectrum of compound **I** were assigned using COSY two-dimensional correlation technique.

Bicyclic *ortho*-aminocarbonitriles I–III (*general procedure*). Morpholine, 0.2 ml (1 mol %), was added to a solution of 0.2 mol of the corresponding cyclic ketone and 30 g (0.2 mol) of benzylidenemalononitrile in 150 ml of methanol, and the mixture was heated for 5 h under reflux. After cooling, the precipitate was filtered off and washed with methanol and petroleum ether.

2-Amino-4-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-1,3,3-tricarbonitrile (I). Yield 27.6 g (46%), mp 261–263°C; published data [4]: mp 259–261°C. IR spectrum, ν, cm^{-1}: 3412, 3341, 3258, 3230 (N–H), 2216 (CN), 1665 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.96 m (1H, 5-H$_A$), 1.43–1.76 m (2H, 6-H), 1.81 m (1H, 5-H$_B$), 2.07–2.37 m (2H, 7-H), 2.88 m (1H, 4a-H), 3.08 d (1H, 4-H, J = 12.5 Hz), 4.87 s (2H, NH$_2$), 6.05 m (1H, 8-H), 7.24–7.65 m (5H, C$_6$H$_5$). Found, %: C 74.32; H 5.04; N 20.97. $C_{19}H_{16}N_4$. Calculated, %: C 74.02; H 5.19; N 20.78.

5-Amino-7-phenyl-3-phenylmethylidene-2,3,6,7-tetrahydro-1*H*-indene-4,6,6-tricarbonitrile (II). Yield 41.2 g (56%), mp 210–211°C. IR spectrum, ν, cm^{-1}: 3420, 3453, 3260, (N–H), 2216 (CN), 1667 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.74–2.81 m (2H, 2-H), 3.04–3.12 m (2H, 1-H), 5.22 s (2H, NH$_2$), 7.26–7.54 m (11H, C$_6$H$_5$, 7-H), 7.86 t (1H, 3-CH, J = 2.5 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 374 (17) [M]$^+$, 347 (68), 256 (25), 165 (23), 91 (100). Found, %: C 79.93; H 5.00; N 15.30. $C_{25}H_{18}N_4$. Calculated, %: C 80.21; H 4.81; N 14.97.

2-Amino-4-phenyl-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-1,3-dicarbonitrile (III). Yield 37.3 g (65%), mp 218°C; published data [5]: mp 220°C. IR spectrum, ν, cm^{-1}: 3410, 3360, 3150 (N–H), 2210 (CN). ^{1}H NMR spectrum, δ, ppm: 1.42–1.56 m (2H, 7-H), 1.66–1.87 m (4H, 6-H, 8-H), 2.46–2.51 m (2H, 5-H), 3.07–3.11 m (2H, 9-H), 5.04 s (2H, NH$_2$), 7.17–7.51 m (5H, C$_6$H$_5$). Mass spectrum, *m*/*z* (I_{rel}, %): 287 (100) [M]$^+$, 258 (23), 245 (20), 230 (23), 77 (17). Found, %: C 79.73; H 5.60; N 14.41. $C_{19}H_{17}N_3$. Calculated, %: C 79.44; H 5.92; N 14.63.

Formimidic acid esters IV and VII (*general procedure*). A mixture of 0.01 mol of compound **I** or **II**, 4 ml (0.024 mol) of triethyl orthoformate, and 0.1 ml (17 mol %) of acetic acid was heated for 3 h under reflux, poured into a Petri dish, and evaporated. The residue can be brought into further syntheses without additional purification. Analytically pure samples were obtained in nearly quantitative yield by column chromatography on aluminum oxide (the products were applied to a column as solutions in chloroform).

Ethyl *N*-(1,3,3-tricyano-4-phenyl-3,4,4a,5,6,7-hexahydronaphthalen-2-yl)formimidate (IV). mp 178–180°C. IR spectrum, ν, cm^{-1}: 2221 (CN), 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.98 m (1H, 5-H$_A$), 1.45 t (3H, CH$_3$, J = 7.2 Hz), 1.45–1.76 m (2H, 6-H), 1.82 m (1H, 5-H$_B$), 2.05–2.42 m (2H, 7-H), 2.91 m (1H, 4a-H), 3.07 d (1H, 4-H, J = 12.6 Hz), 4.42 q (2H, OCH$_2$, J = 7.2 Hz), 6.41 m (1H, 8-H), 7.21–7.62 m (5H, C$_6$H$_5$), 7.95 s (1H, CH=N). Found, %: C 74.43; H 5.50; N 15.42. $C_{22}H_{20}N_4O$. Calculated, %: C 74.15; H 5.62; N 15.73.

Ethyl *N*-(4,6,6-tricyano-7-phenyl-3-phenylmethylidene-2,3,6,7-tetrahydro-1*H*-inden-5-yl)formimidate (VII). mp 198–199°C. IR spectrum, ν, cm^{-1}: 2223 (CN), 1637 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.46 t (3H, CH$_3$, J = 7.3 Hz), 2.78–2.90 m (2H, 2-H), 3.07–3.18 m (2H, 1-H), 4.50 q (2H, OCH$_2$, J = 7.3 Hz), 7.27–7.54 m (11H, C$_6$H$_5$, 7-H), 7.90 s (1H, CH=N), 7.96 t (1H, 3-CH, J = 2.5 Hz). Found, %: C 78.43; H 5.40; N 12.82. $C_{28}H_{22}N_4O$. Calculated, %: C 78.14; H 5.12; N 13.02.

Amidines V and VIII (*general procedure*). A solution of 3 mmol of compound **IV** or **VII** and 0.26 ml (3 mmol) of morpholine in 30 ml of benzene was heated for 3 h under reflux. The mixture was cooled and subjected to chromatography on aluminum oxide using benzene as eluent; the products were recrystallized from petroleum ether.

2-Morpholinomethylideneamino-4-phenyl-3,4,4a,5,6,7-hexahydronaphthalene-1,3,3-tricarbonitrile (V). Yield 0.92 g (78%), mp 214–216°C. IR spectrum, ν, cm^{-1}: 2220 (CN), 1623 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.97 m (1H, 5-H$_A$), 1.42–1.73 m (2H, 6-H), 1.73 m (1H, 5-H$_B$), 2.10–2.40 m (2H, 7-H), 2.86 m (1H, 4a-H), 3.03 d (1H, 4-H, J = 12.5 Hz), 3.47–3,90 m (8H, CH$_2$, morpholine), 6.24 m (1H, 8-H), 7.24–7.63 m (5H, C$_6$H$_5$), 7.89 s (1H, CH=N). Found, %: C 73.63; H 4.41; N 17.52. $C_{24}H_{18}N_5O$. Calculated, %: C 73.47; H 4.59; N 17.86.

5-Morpholinomethylideneamino-7-phenyl-3-phenylmethylideneindan-4,6-dicarbonitrile (VIII). Yield 0.87 g (65%), mp 192–194°C. IR spectrum, ν,

cm^{-1}: 2222 (CN), 1622 (C=C). ^1H NMR spectrum, δ, ppm: 2.78–2.86 m (2H, 2-H), 3.04–3.16 m (2H, 1-H), 3.42–3.92 m (8H, CH_2, morpholine), 7.27–7.58 m (10H, C_6H_5), 7.77 s (1H, CH=N), 7.97 t (1H, 3-CH, J = 2.5 Hz). Mass spectrum, m/z (I_{rel}, %): 444 (50) $[M]^+$, 413 (10), 347 (10), 99 (15), 86 (100). Found, %: C 78.66; H 5.21; N 12.33. $C_{29}H_{24}N_4O$. Calculated, %: C 78.38; H 5.40; N 12.61.

2-Benzyl-1-imino-6-phenyl-1,2,5,6,6a,7,8,9-octahydrobenzo[*f*]quinazoline-5,5-dicarbonitrile (VI). A solution of 1.1 g (0.03 mol) of compound **V** and 0.33 ml (0.03 mol) of benzylamine in 20 ml of benzene was heated for 1 h under reflux, 5 mg (30 mol %) of sodium methoxide was added, and the mixture was heated for 4 h under reflux, cooled, and subjected to chromatography on aluminum oxide using benzene as eluent. The product was recrystallized from methanol. Yield 0.90 g (72%), mp 174–175°C. IR spectrum, ν, cm^{-1}: 3335 (N–H), 2223 (CN), 1632 (C=C). ^1H NMR spectrum, δ, ppm: 0.91 m (1H, 7-H_A), 1.18–1.51 m (2H, 8-H), 1.79 m (1H, 7-H_B), 2.10–2.42 m (2H, 9-H), 2.82–2.96 m (2H, 6-H, 6a-H), 4.81 d (1H, NCH_2, J = 15.1 Hz), 4.92 d (1H, NCH_2, J = 15.1 Hz), 6.44 m (1H, 10-H), 7.21–7.56 m (10H, C_6H_5), 7.94 d (1H, NH), 8.85 s (1H, 3-H). Found, %: C 77.56; H 5.34; N 16.57. $C_{27}H_{23}N_5$. Calculated, %: C 77.70; H 5.51; N 16.79.

The ^1H NMR spectra were recorded on a Varian VXR-300 spectrometer at 300 MHz from solutions in chloroform-*d*.

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