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Reactions of octahydroacridine-4-carbonitrile (carboxamide) with electrophilic reagents

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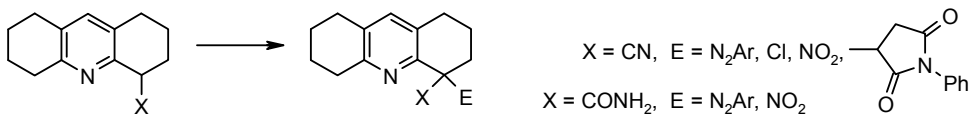


Octahydroacridine-4-carbonitrile (carboxamide) was shown to react with aryldiazonium salts and other electrophilic reagents in acidic and neutral media. The reactions occurred at the methine carbon atom, forming the corresponding 4-functionalized derivatives. The obtained azo compounds decomposed at 140–155°C with elimination of nitrogen and gave products formed by the reactions of radical intermediates.

Keywords: diazonium salt, octahydroacridines, azo coupling, electrophilic substitution, Japp–Klingemann reaction, radical, radical reactions.

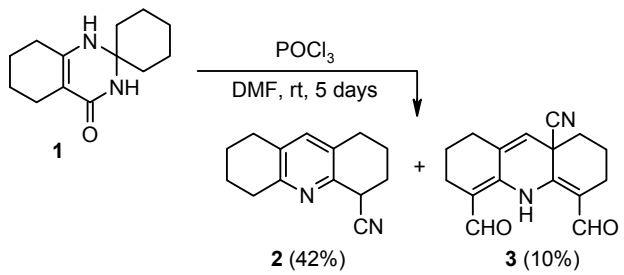
We have previously described a nontrivial transformation of 5',6',7',8'-tetrahydro-1'*H*-spiro[cyclohexane-1,2'-quinazolin]-4'(3'*H*)-one (**1**) to hydroacridine derivatives **2** and **3** that formed under Vilsmeier–Haack reaction conditions (Scheme 1).[1] 1,2,3,4,5,6,7,8-Octahydroacridine-4-carbonitrile (**2**) was easily isolated from the reaction product mixture by extraction with methanol, providing a relatively easy access to this compound.

Preliminary study of the chemical properties of nitrile **2** showed that it reacted quite readily in azo coupling with diazonium salts containing an activating nitro group.[2] Further investigation showed that unactivated diazonium salts obtained from toluidine and aniline can also participate in azo coupling reactions. Prior to our work there were three examples of similar transformations described in the literature, namely, interaction of 1,2,3,4-tetrahydroacridine-4-carbonitrile and 2,3-dihydro-1*H*-cyclopenta[*b*]quinoline-3-carbonitrile with diazonium salts.[3] In the current work we established that this reaction is generally applicable, and the nature of substituents in the aryl ring of diazonium salts can be varied widely, producing azo coupling products **4a**–**h** in 40–70% yields (Scheme 2).

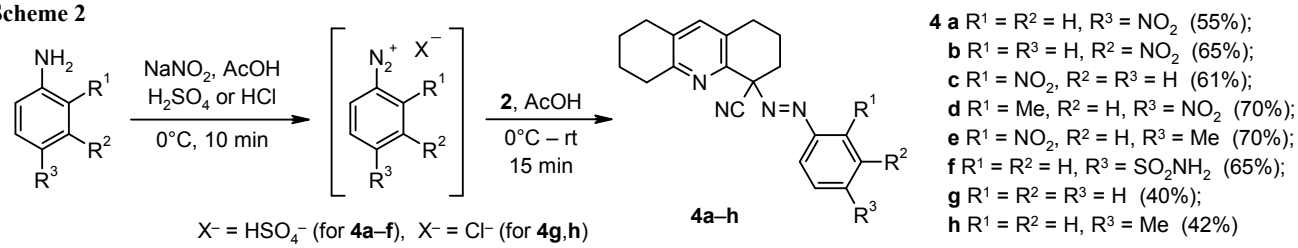
We should note that compounds **4a**–**h** are easily isolated from the reaction medium and do not require additional purification. Also, unlike the standard azo coupling conditions in alkaline medium, the reaction in the case of octahydroacridine **2** occurred easily in acidic medium. In our opinion, this can be explained by tautomerism of substrate **2**, resulting in the generation of nucleophilic enamine center, susceptible to electrophilic attack by diazonium salt (Scheme 3).

As known from the literature,[4] coupling reaction with diazonium salts leading to the formation of arylhydrazones in the presence of a large excess of base in ethanol can also be achieved with (4-nitrophenyl)acetonitrile, while alternative

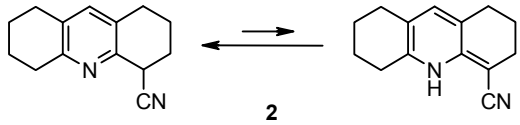
Scheme 1



Scheme 2



Scheme 3



routes were employed for the preparation of hydrazones from benzyl cyanide.[4–8] Comparing the conditions and results of these reactions with azo coupling of compounds **2**, we can conclude that the pyridine ring in the structure of compound **2** substantially facilitates azo coupling reactions.

Amide **5**, readily available by acidic hydrolysis of nitrile **2**,[2] also participated in azo coupling reaction, which occurred analogously in acetic acid (Scheme 4).

A reaction of diazonium salts with β-dicarbonyl compounds in the presence of bases (Japp–Klingemann reaction) is known in the literature.[9] Elimination of one carbonyl group usually occurs under these conditions and hydrazones are formed instead of azo compounds. In our case, in a mixture of acetic, nitrous, and hydrochloric acids, elimination of the amide group did not occur, but azo compounds **6a**,**b** were formed instead (Scheme 4).

The elimination of amide group with the formation of aryl hydrazones **7a**,**b** occurred in the presence of a significant amount of concentrated sulfuric acid (Scheme 4). According to ^{1}H data acquired in DMSO-d_6, compounds **7a**,**b** existed as single isomers assumed to be the *E*-isomer, indirectly indicated by the chemical shifts of NH protons at 10.77 and 10.18 ppm, respectively.[10]

The structures of azo compounds **4a**–**d** were proposed based on the analysis of IR and ^{1}H NMR spectra, as well as mass spectra. X-ray structural analysis was performed for compound **4c**, confirming the proposed structure (Fig. 1). Two cyclohexene rings in the structure **4c** formed a distorted-chair conformation with C(3), C(4), C(10), and C(11) atoms deviating from the median plane of other ring atoms by

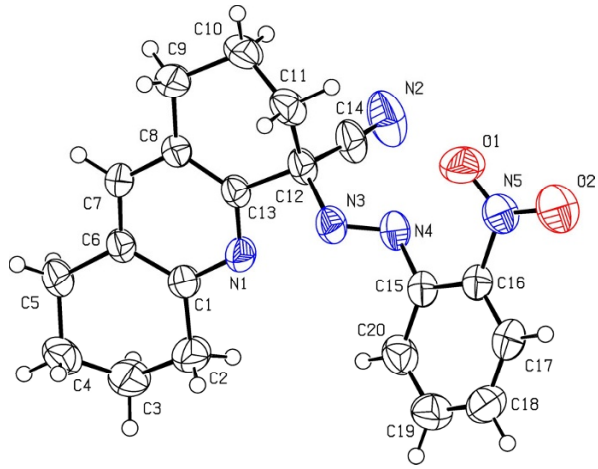
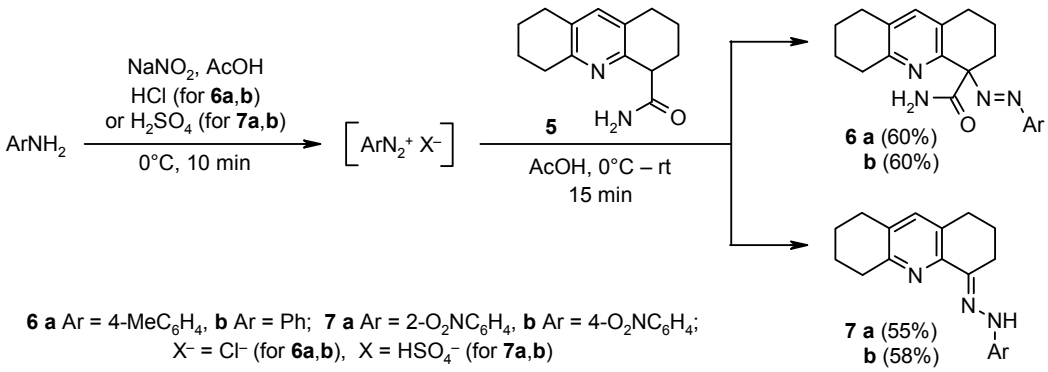


Figure 1. The structure of compound **4c** represented as non-hydrogen atoms by thermal vibration ellipsoids of 50% probability.

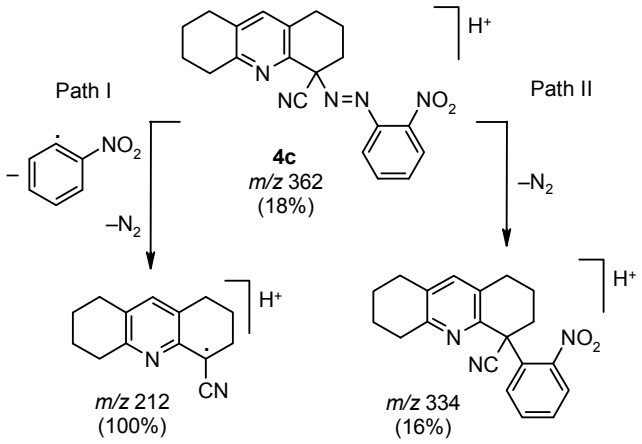
–0.23, 0.49, –0.30, and 0.45 Å, respectively. The nitrile substituent was oriented axially relative to the partially saturated ring (the torsion angle C(8)–C(13)–C(12)–C(14) was –101.55(17)°). The nitro group was only slightly rotated relative to the benzene ring (the torsion angle N(5)–C(16)–C(17)–O(2) was –9.18(13)°), which led to steric repulsion between the *ortho* substituents of the aromatic ring. This was evidenced by the shortened intramolecular contact N(4)···O(1) 2.60 Å (sum of van der Waals radii 2.79 Å)[11] and the increase of valence angles N(4)–C(15)–C(16) 121.98(16)°, C(15)–C(16)–N(5) 120.19(6)°, and N(5)–C(16)–C(17) 118.23(16)°.

An additional structural proof for the synthesized azo compounds can be obtained from the mass spectral fragmentation patterns, presented for the example of compound **4c** (FAB ionization) (Scheme 5).

Scheme 4

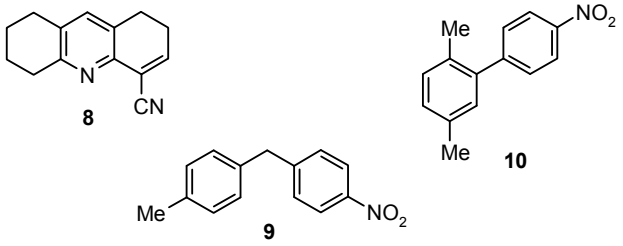


Scheme 5



The major fragmentation route for these compounds is the elimination of nitrogen molecule and aryl radical, forming radical ions with *m*/*z* 212 (100%) (Route I). The elimination of nitrogen molecule with further recombination of the radical intermediates (leading to nonradical ions with *m*/*z* 334 (16%) for compound **4c** (Route II)) was found to be a minor mode of fragmentation. We should note that fragmentation according to Route II was not observed for compound **4a**.

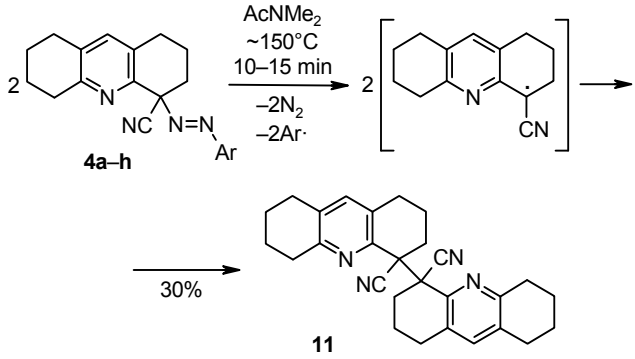
The obtained azo compounds **4a**–**h** decomposed with elimination of nitrogen molecule also when heated to 140–155°C. We studied the thermal decomposition of these compounds by heating in various solvents. Thus, thermolysis of compound **4a** in refluxing *p*-xylene gave the following products according to GC-MS: octahydroacridine-4-carbonitrile **2** (retention time t_R 3.97 min, *m*/*z* 212 $[M]^+$), dehydrogenated analog **8** (t_R 4.61 min, *m*/*z* 210 $[M]^+$), and products from aryl radical reactions, compounds **9** and **10** (t_R 3.10 and 3.35 min, *m*/*z* 227 $[M]^+$). The obtained compounds could not be isolated in analytically pure form.



Radicals are well known for their high reactivity and typically do not leave their solvent cage. This results in reactions with *p*-xylene, which is capable of forming a stabilized "benzyl" radical, thus producing compound **9**. The isomeric compound **10** was formed during arylation of *p*-xylene according to a Gomberg–Bachmann type reaction.[12]

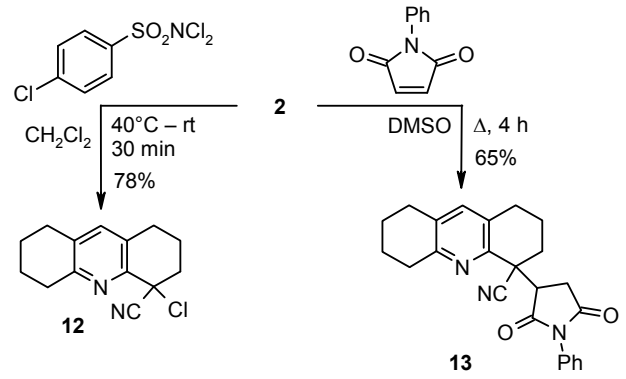
In order to avoid solvent participation in the reaction, the process was performed in *N*,*N*-dimethylacetamide. After thermolysis of compounds **4a**–**h** in this solvent, HPLC-MS data for the reaction mixture showed not only signals of compounds **2** (t_R 1.02 min) and **8** (t_R 1.27 min), but also a signal with *m*/*z* 423.1 $[M+H]^+$ (t_R 1.65 min), corresponding to a compound generated by recombination of two cyanoacridine radicals. We were able to isolate this product as individual compound. Based on the analysis of ^{1}H NMR and mass spectra, we identified its structure as compound **11** (Scheme 6).

Scheme 6



As shown above, the mutual influence of pyridine ring and nitrile group in compound **2** sufficiently increased the reactivity of its C-4 atom, enabling reactions with such electrophilic reagents as diazonium salts. For this reason, we were interested in studying the behavior of nitrile **2** also in reactions with other electrophiles. Thus, *N*,*N*-dichloroamide of *p*-chlorobenzenesulfonic acid and *N*-phenylmaleimide were used in reactions with nitrile **2**. As expected, the reaction products were compounds **12** and **13**, respectively. Previously we described an analogous reaction of nitrile **2** with acrylonitrile (Scheme 7).[13]

Scheme 7

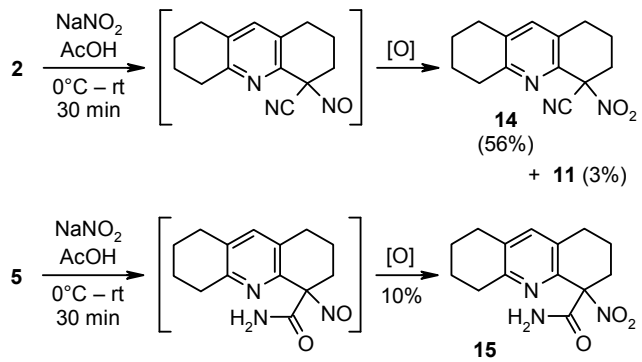


An interesting and unexpected result was obtained from nitrosation of nitrile **2** with sodium nitrite in acetic acid. Instead of the expected nitroso compound, a mixture was obtained that consisted of mostly the nitro derivative **14** and a small amount of dimer **11** (~3%) (Scheme 8). The structure of reaction products was established based on the analysis of IR and ^{1}H NMR spectra, as well as mass spectra of the isolated mixture.

We conclude that the nitro compound **14** was formed by oxidation of intermediate nitroso compound, because the initial reaction mixture immediately after addition of sodium nitrite to substrate **2** was bright-green, but turned yellow towards the end of reaction. We were not able to isolate the nitroso compound. The dimer **11** was clearly formed by a radical mechanism. The cyanoacridine radical, which underwent further dimerization, was likely formed by elimination of hydrogen atom from the nitrile **2** through reaction with nitrogen dioxide.

The amide **5** was nitrated analogously, but due to its lower stability under the reaction conditions, the yield of nitro derivative **15** did not exceed 10% (Scheme 8).

Scheme 8



Thus, we have shown in this work that the mutual influence of pyridine ring and nitrile (amide) group increased the reactivity of nitrile and amide derived from 1,2,3,4,5,6,7,8-octahydroacridine-4-carboxylic acid at position 4, allowing to perform reactions with various electrophilic reagents in acidic and neutral media. We also established that nitrosation of these compounds with nitrous acid gave nitrile and amide of 4-nitro-1,2,3,4,5,6,7,8-octahydroacridine-4-carboxylic acid.

Experimental

IR spectra were recorded on a Perkin Elmer Spectrum One spectrophotometer in KBr pellets. ^{1}H NMR spectra were acquired on Bruker Avance II 400 (400 MHz) (compounds **4c**,**d**,**g**,**h, 6a**,**b**, **7a**, **11**, **13**, **14**) or Varian VXR-200 (200 MHz) instruments (the rest of the compounds). Solvents: 10:1 DMSO-d_6–CCl_4, (compound **13**) or DMSO-d_6 (the rest of the compounds), internal standard TMS. One-dimensional ^{13}C, as well as ^{13}C DEPT-135 NMR spectra were acquired on a Bruker Avance II 400 instrument at 100 MHz (compound **13**) in 10:1 DMSO-d_6–CCl_4 solution, internal standard TMS. Mass spectra with EI ionization were recorded on an MX1321 instrument (compounds **11**, **12**, **15**) with direct introduction of sample into the ion source at ionization chamber temperature 200°C and ionizing electron energy of 70 eV. The FAB spectra of other compounds were recorded on a VG7070 spectrometer. Desorption of ions from sample solution in *m*-nitrobenzyl alcohol and thioglycerol (compound **4g**) was performed with a beam of 8 keV argon atoms. Elemental analysis was performed on a LECO CHNS-900 instrument. Melting points were determined with a Thiele apparatus. The reaction progress and purity of the obtained compounds were controlled by TLC on Merck Silicagel 60 F_{254} plates with 10:1 $CHCl_3$–2-PrOH mobile phase. The HPLC-MS analysis was performed on an Agilent 1200 instrument, with Rapid Resolution HT Cartrige 4.6 × 30 mm column, 1.8 μm, Zorbax SB-C18, DAD and MS detectors, electrospray ionization at atmospheric pressure. The GC-MS analysis was performed on a Varian 1200L gas chromato-mass spectrometer (EI ionization, 70 eV), Optima-5 capillary column (Macherey-Nagel), stationary phase – 5% phenylpolysiloxane and 95% dimethylpolysiloxane.

4-[(*E*)-(4-Nitrophenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4a). Concentrated (96%) sulfuric acid (2.77 ml, 0.05 mol) was stirred with overhead stirrer and cooled with ice bath. Dry sodium nitrite (1.38 g, 0.02 mol) and *p*-nitroaniline (1.38 g, 0.01 mol) in AcOH (30 ml) were added, the mixture was stirred for 10 min. A solution of nitrile **2** (2.12 g, 0.01 mol) in AcOH (15 ml) was added dropwise to the obtained diazonium salt with cooling in ice bath. The mixture was stirred for 15 min, diluted with H_2O (50 ml), and neutralized with 1 N K_2CO_3 solution to pH 8–9. The yellow precipitate was filtered off and recrystallized from 2-PrOH. Yield 2.00 g (55%). Yellow powder. Mp 135–136°C (decomp.). IR spectrum, ν, cm^{-1}: 2929–2857 (–$(CH_2)_n$–), 2241 (CN), 1525, 1349 (NO_2), 1449 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65–2.27 (6H, m, 2,6,7-CH_2); 2.53–2.75 (6H, m, 1,3,8-CH_2); 2.93–2.97 (2H, m, 5-CH_2); 7.45 (1H, s, H-9); 7.91 (2H, d, ^3J = 9.0, H-2,6 Ar); 8.38 (2H, d, ^3J = 9.0, H-3,5 Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 362 $[M+H]^+$ (26), 212 $[M+H–N_2C_6H_4NO_2]^+$ (56). Found, %: C 66.56; H 5.34; N 19.42. $C_{20}H_{19}N_5O_2$. Calculated, %: C 66.47; H 5.30; N 19.38.

Compounds **4b–f**, **7a**,**b** were obtained analogously; H_2SO_4 was substituted with an equivalent excess of conc. HCl for the preparation of compounds **4g**,**h**, **6a**,**b**.

4-[(*E*)-(3-Nitrophenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4b). Yield 65%. Yellow powder. Mp 140–141°C (decomp.). IR spectrum, ν, cm^{-1}: 2935 (–$(CH_2)_n$–), 2231 (CN), 1535, 1351 (NO_2), 1453 (–N=N–). ^{1}H NMR spectrum, δ, ppm: 1.65–2.27 (6H, m, 2,6,7-CH_2); 2.53–2.75 (6H, m, 1,3,8-CH_2); 2.90–2.97 (2H, m, 5-CH_2); 7.45 (1H, s, H-9); 7.82–7.91 (1H, m, H-5 Ar); 8.21–8.25 (1H, m, H-6 Ar); 8.28–8.34 (1H, m, H-2 Ar); 8.38–8.46 (1H, m, H-4 Ar). Mass spectrum, *m*/*z* (I_{rel}, %): 362 $[M+H]^+$ (10), 334 $[M+H–N_2]^+$ (6), 212 $[M+H–N_2C_6H_4NO_2]^+$ (100). Found, %: C 66.58; H 5.35; N 19.45. $C_{20}H_{19}N_5O_2$. Calculated, %: C 66.47; H 5.30; N 19.38.

4-[(*E*)-(2-Nitrophenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4c). Yield 61%. Red needles. Mp 142–143°C (decomp.). IR spectrum, ν, cm^{-1}: 2957 (–$(CH_2)_n$–), 2236 (CN), 1515, 1345 (NO_2), 1452 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66–1.82 (4H, m, 6,7-CH_2); 1.91–2.01 (1H, m, 2-CH_{ax}); 2.15–2.24 (1H, m, 2-CH_{eq}); 2.38–2.48 (2H, m, 1(8)-CH_2); 2.61–2.79 (4H, m, 3-CH_2, 8(1)-CH_2); 2.89–2.93 (2H, m, 5-CH_2); 7.35 (1H, d, ^3J = 7.7, H-6 Ar); 7.42 (1H, s, H-9); 7.71–7.90 (2H,

m, H-4,5 Ar); 8.14 (1H, d, ^3J = 7.8, H-3 Ar). Mass spectrum, *m/z* (I_{rel}, %): 362 $[M+H]^+$ (18), 334 $[M+H-N_2]^+$ (16), 212 $[M+H-N_2C_6H_4NO_2]^+$ (100). Found, %: C 66.55; H 5.34; N 19.43. $C_{20}H_{19}N_5O_2$. Calculated, %: C 66.47; H 5.30; N 19.38.

4-[(*E*)-(2-Methyl-4-nitrophenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4d). Yield 70%. Yellow powder. Mp 145–146°C (decomp.). IR spectrum, ν, cm^{-1}: 2934 (–$(CH_2)_n$–, CH_3), 2234 (CN), 1526, 1344 (NO_2), 1452 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66–1.82 (4H, m, 6,7-CH_2); 1.91–2.01 (1H, m, 2-CH_{ax}); 2.15–2.24 (1H, m, 2-CH_{eq}); 2.38–2.48 (2H, m, 1(8)-CH_2); 2.56–2.65 (2H, m, 8(1)-CH_2); 2.68–2.77 (5H, m, 3-CH_2, CH_3); 2.89–2.95 (2H, m, 5-CH_2); 7.44 (1H, s, H-9); 7.73 (1H, d, ^3J = 8.5, H-6 Ar); 7.91 (1H, d, ^4J = 2.4, H-3 Ar); 8.29 (1H, dd, ^3J = 8.5, ^4J = 2.4, H-5 Ar). Mass spectrum, *m/z* (I_{rel}, %): 376 $[M+H]^+$ (13), 348 $[M+H-N_2]^+$ (15), 212 $[M+H-N_2C_6H_3(CH_3)NO_2]^+$ (100). Found, %: C 67.27; H 5.69; N 18.72. $C_{21}H_{21}N_5O_2$. Calculated, %: C 67.18; H 5.64; N 18.65.

4-[(*E*)-(4-Methyl-2-nitrophenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4e). Yield 70%. Yellow powder. Mp 145–146°C (decomp.). IR spectrum, ν, cm^{-1}: 2944 (–$(CH_2)_n$–, CH_3), 2235 (CN), 1520, 1348 (NO_2), 1454 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65–2.27 (6H, m, 2,6,7-CH_2); 2.44 (3H, s, CH_3); 2.53–2.78 (6H, m, 1,3,8-CH_2); 2.87–2.93 (2H, m, 5-CH_2); 7.31 (1H, d, ^3J = 8.2, H-5 Ar); 7.42 (1H, s, H-9); 7.62 (1H, d, ^3J = 8.2, H-6 Ar); 7.96 (1H, s, H-3 Ar). Mass spectrum, *m/z* (I_{rel}, %): 376 $[M+H]^+$ (26), 348 $[M+H-N_2]^+$ (37), 212 $[M+H-N_2C_6H_3(CH_3)NO_2]^+$ (100). Found, %: C 67.11; H 5.58; N 18.60. $C_{21}H_{21}N_5O_2$. Calculated, %: C 67.18; H 5.64; N 18.65.

4-[(*E*)-(4-Cyano-1,2,3,4,5,6,7,8-octahydroacridin-4-yl)-diazenyl]benzenesulfonamide (4f). Yield 65%. Pale-yellow powder. Mp 180–181°C (decomp.). IR spectrum, ν, cm^{-1}: 3390 (NH_2), 2923 (–$(CH_2)_n$–), 2230 (CN), 1454 (–N=N–), 1350, 1165–1152 (SO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65–2.26 (6H, m, 2,6,7-CH_2); 2.53–2.75 (6H, m, 1,3,8-CH_2); 2.92–2.97 (2H, m, 5-CH_2); 7.45 (1H, s, H-9); 7.55 (2H, s, NH_2); 7.86 (2H, d, ^3J = 7.9, H-3,5 Ar); 7.98 (2H, d, ^3J = 7.9, H-2,6 Ar). Mass spectrum, *m/z* (I_{rel}, %): 396 $[M+H]^+$ (7), 368 $[M+H-N_2]^+$ (15), 212 $[M+H-N_2C_6H_4SO_2NH_2]^+$ (96). Found, %: C 60.89; H 5.41; N 17.75. $C_{20}H_{21}N_5O_2S$. Calculated, %: C 60.74; H 5.35; N 17.71.

4-[(*E*)-Phenyldiazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4g). Yield 40%. Yellow powder. Mp 125–126°C (decomp.). IR spectrum, ν, cm^{-1}: 2931–2861 (–$(CH_2)_n$–), 2242 (CN), 1450 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66–1.82 (4H, m, 6,7-CH_2); 1.91–2.01 (1H, m, 2-CH_{ax}); 2.15–2.25 (1H, m, 2-CH_{eq}); 2.36–2.48 (2H, m, 1(8)-CH_2); 2.58–2.70 (2H, m, 8(1)-CH_2); 2.71–2.77 (2H, m, 3-CH_2); 2.93 (2H, t, ^3J = 6.2, 5-CH_2); 7.42 (1H, s, H-9); 7.52–7.57 (3H, m, H Ph); 7.66–7.72 (2H, m, H Ph). Mass spectrum, *m/z* (I_{rel}, %): 317 $[M+H]^+$ (12), 289 $[M+H-N_2]^+$ (5), 212 $[M+H-N_2Ph]^+$ (100). Found, %: C 75.81; H 6.30; N 17.66. $C_{20}H_{20}N_4$. Calculated, %: C 75.92; H 6.37; N 17.71.

4-[(*E*)-(4-Methylphenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (4h). Yield 42%. Yellow powder. Mp 133–134°C (decomp.). IR spectrum, ν, cm^{-1}: 2937–2835 (–$(CH_2)_n$–, CH_3), 2232 (CN), 1454 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66–1.79 (4H, m, 6,7 CH_2); 1.88–2.01 (1H, m, 2-CH_{ax}); 2.13–2.25 (1H, m, 2-CH_{eq}); 2.37 (3H, s, CH_3); 2.38–2.48 (2H, m, 1(8)-CH_2); 2.55–2.70 (2H, m, 8(1)-CH_2); 2.71–2.76 (2H, m, 3-CH_2); 2.92 (2H, t, ^3J = 6.2, 5-CH_2); 7.35 (2H, d, ^3J = 7.6, H-3,5 Ar); 7.41 (1H, s, H-9); 7.61 (2H, d, ^3J = 7.6, H-2,6 Ar). Mass spectrum, *m/z* (I_{rel}, %): 331 $[M+H]^+$ (12), 303 $[M+H-N_2]^+$ (9), 212 $[M+H-N_2C_6H_4Me]^+$ (67). Found, %: C 76.43; H 6.80; N 17.05. $C_{21}H_{22}N_4$. Calculated, %: C 76.33; H 6.71; N 16.96.

4-[(*E*)-(4-Methylphenyl)diazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carboxamide (6a). Yield 60%. Yellow powder. Mp 145–146°C (decomp.). IR spectrum, ν, cm^{-1}: 3433 (NH_2), 2930–2852 (–$(CH_2)_n$–, CH_3), 1678 (CO), 1436 (–N=N–). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.52–1.78 (6H, m); 2.05–2.12 (1H, m); 2.34 (3H, s, CH_3); 2.51–2.73 (7H, m); 7.19 (1H, s, H-9); 7.28 (2H, d, ^3J = 8.4, H-3,5 Ar); 7.54 (1H, br. s) and 7.58 (1H, br. s, NH_2); 7.56 (2H, d, ^3J = 8.4, H-2,6 Ar). Mass spectrum, *m/z* (I_{rel}, %): 349 $[M+H]^+$ (21), 230 $[M+H-N_2C_6H_4Me]^+$ (100). Found, %: C 72.28; H 6.88; N 16.02. $C_{21}H_{24}N_4O$. Calculated, %: C 72.39; H 6.94; N 16.08.

4-[(*E*)-Phenyldiazenyl]-1,2,3,4,5,6,7,8-octahydroacridine-4-carboxamide (6b). Yield 60%. Yellow powder. Mp 140–141°C (decomp.). IR spectrum, ν, cm^{-1}: 3451 (NH_2), 2919–2828 (–$(CH_2)_n$–), 1685 (CO), 1452 (–N=N–). ^{1}H NMR spectrum, δ, ppm: 1.52–1.78 (6H, m); 2.05–2.15 (1H, m); 2.33–2.43 (1H, m); 2.56–2.72 (6H, m); 7.20 (1H, s, H-9); 7.45–7.51 (3H, m, H Ph); 7.56 (1H, s) and 7.58 (1H, s, NH_2); 7.62–7.68 (2H, m, H Ph). Mass spectrum, *m/z* (I_{rel}, %): 335 $[M+H]^+$ (24), 230 $[M+H-N_2Ph]^+$ (100). Found, %: C 71.95; H 6.70; N 16.81. $C_{20}H_{22}N_4O$. Calculated, %: C 71.83; H 6.63; N 16.75.

(2-Nitrophenyl)hydrazone of (4*E*)-2,3,5,6,7,8-hexahydroacridin-4(1*H*)-one (7a). Yield 55%. Red powder. Mp 236–238°C. IR spectrum, ν, cm^{-1}: 3310 (NH), 2932–2858 (–$(CH_2)_n$–), 1614 (C=N), 1578, 1328 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.65–1.95 (6H, m, 2,6,7-CH_2); 2.62–2.88 (8H, m, 1,3,5,8-CH_2); 6.94 (1H, t, ^3J = 7.7, H-4 Ar); 7.25 (1H, s, H-9); 7.71 (1H, t, ^3J = 8.0, H-5 Ar); 8.02 (1H, d, ^3J = 8.3, H-6 Ar); 8.13 (1H, d, ^3J = 8.7, H-3 Ar); 10.77 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 337 $[M+H]^+$ (100). Found, %: C 67.96; H 6.07; N 16.73. $C_{19}H_{20}N_4O_2$. Calculated, %: C 67.84; H 5.99; N 16.65.

(4-Nitrophenyl)hydrazone of (4*E*)-2,3,5,6,7,8-hexahydroacridin-4(1*H*)-one (7b). Yield 58%. Yellow powder. Mp 250–253°C. IR spectrum, ν, cm^{-1}: 3436 (NH), 2937–2856 (–$(CH_2)_n$–), 1597 (C=N), 1567, 1319 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.64–1.92 (6H, m, 2,6,7-CH_2); 2.62–2.88 (8H, m, 1,3,5,8-CH_2); 7.23 (1H, s, H-9); 7.36 (2H, d, ^3J = 9.1, H-2,6 Ar); 8.13 (2H, d, ^3J = 9.1, H-3,5 Ar); 10.18 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 337 $[M+H]^+$ (100). Found, %: C 67.98; H 6.05; N 16.72. $C_{19}H_{20}N_4O_2$. Calculated, %: C 67.84; H 5.99; N 16.65.

Thermolysis of compound 4a. Method I. A solution of compound **4a** (1 g, 3 mmol) in *p*-xylene (7 ml) was refluxed for 10–15 min, then the mixture was cooled to room temperature, diluted with *n*-hexane (5 ml), and analyzed by GC-MS.

Thermolysis of compounds 4a–h. Method II. Thermolysis was performed analogously to method I, using *N*,*N*-dimethylacetamide as solvent and maintaining the reaction temperature at approximately 150°C. After cooling to room temperature, water was added to the reaction mixture, and the precipitate that formed was filtered off. The obtained product was analyzed without purification by HPLC-MS or recrystallized from *n*-hexane, giving **2,2',3,3',5,5',6,6',7,7',8,8-dodecahydro-4,4'-diacridine-4,4'(1*H*,1'*H*)-dicarbonitrile (11)**. Yield 30%. Orange powder. Mp 130–133°C. ^{1}H NMR spectrum, δ, ppm: 1.52–1.93 (12H, m, 6CH_2); 2.52–2.87 (16H, m, 8CH_2); 7.23 (2H, s, H-9,9'). Mass spectrum, *m*/*z* (I_{rel}, %): 422 $[M]^+$ (11). Found, %: C 79.79; H 7.25; N 13.35. $C_{28}H_{30}N_4$. Calculated, %: C 79.59; H 7.16; N 13.26.

4-Chloro-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (12). *N*,*N*-Dichloroamide of *p*-chlorobenzenesulfonic acid (2.60 g, 0.01 mol) was dissolved in CH_2Cl_2 (5 ml) and gradually added to a solution of compound **2** (2.12 g, 0.01 mol) in CH_2Cl_2 (5 ml), resulting in exothermic effect that brought the reaction mixture to boiling. The mixture was vigorously stirred for 30 min, then treated with 20% Na_2SO_3 solution (5 ml). The organic layer was separated, dried over Na_2SO_4, and evaporated to dryness under vacuum. The residue was recrystallized from *n*-hexane. Yield 1.92 g (78%). Colorless powder. Mp 80–83°C. IR spectrum, ν, cm^{-1}: 2983–2831 (–$(CH_2)_n$–), 2245 (CN). ^{1}H NMR spectrum, δ, ppm: 1.53–2.03 (6H, m, 2,6,7-CH_2); 2.55–2.93 (8H, m, 1,3,5,8-CH_2); 7.35 (1H, s, H-9). Mass spectrum, *m*/*z* (I_{rel}, %): 248 $[M(^{37}Cl)]^+$ (4), 246 $[M(^{35}Cl)]^+$ (12), 211 $[M–Cl]^+$ (100), 184 $[M–Cl–HCN]^+$ (37). Found, %: C 68.05; H 6.08; N 11.08. $C_{14}H_{15}ClN_2$. Calculated, %: C 68.15; H 6.13; N 11.35.

4-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (13). *N*-Phenylmaleimide (1.73 g, 0.01 mol) was added to a solution of compound **2** (2.12 g, 0.01 mol) in DMSO (5 ml). The reaction mixture was refluxed for 4 h, cooled to room temperature, diluted with a small amount of water and allowed to crystallize for 1 day. The precipitate that formed was filtered off. Yield 2.5 g (65%). Beige needles. Mp 154–156°C (DMF–H_2O). IR spectrum, ν, cm^{-1}: 2938–2854 (–$(CH_2)_n$–), 2234 (CN), 1711 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.59–2.09 (6H, m, 3CH_2); 2.35–2.40 (1H, m); 2.51–2.85 (7H, m); 3.02–3.16 (1H, m); 3.33–3.43 (1H, m); 3.70–3.75 (1H, m); 6.91 (2H, d, ^3J = 7.5, H-2,6 Ph); 7.23 (1H, s, H-9); 7.31–7.42 (3H, m, H-3,4,5 Ph). ^{13}C NMR spectrum, δ, ppm: 19.7 (CH_2); 22.1 (CH_2); 22.3 (CH_2); 26.9 (CH_2); 27.6 (CH_2); 31.4 (CH_2); 32.3 (CH_2); 34.9 (CH_2 pyrrolidine); 43.2 (C-4); 45.7 (CH pyrrolidine); 120.8 (CN); 126.1 (CH Ph); 127.6 (CH Ph); 128.1 (CH Ph); 129.4 (C Ph); 131.8 (C Py); 131.9 (C Py); 138.1 (C-9); 148.1 (C Py); 154.6 (C Py); 174.2 (CO); 174.7 (CO). DEPT-135 ^{13}C NMR spectrum, δ, ppm: 19.7* (CH_2); 22.1* (CH_2); 22.3* (CH_2); 26.9* (CH_2); 27.6* (CH_2); 31.4* (CH_2); 32.3* (CH_2); 34.9* (CH_2 pyrrolidine); 45.7 (CH pyrrolidine); 126.1 (CH Ph); 127.6 (CH Ph); 128.1 (CH Ph); 138.1 (C-9). Mass spectrum, *m*/*z* (I_{rel}, %): 386 $[M+H]^+$ (100), 359 $[M+H–HCN]^+$ (6). Found, %: C 74.90; H 6.09; N 10.97. $C_{24}H_{23}N_3O_2$. Calculated, %: C 74.78; H 6.01; N 10.90.

* Signal in antiphase.

4-Nitro-1,2,3,4,5,6,7,8-octahydroacridine-4-carbonitrile (14). A solution of compound **2** (2.12 g, 10 mmol) in AcOH (20 ml) was stirred and cooled in ice bath, while dry $NaNO_2$ (3.00 g, 43 mmol) was gradually added. The mixture was maintained at room temperature for 30 min, then poured onto crushed ice and neutralized with 15% ammonia solution to pH 8–9. The precipitate that formed was filtered off and recrystallized from MeOH. The product was colorless powder (1.5 g), containing compound **14** (56% yield) with impurity of dimer **11** (~3% yield), according to ^{1}H NMR data. Mp 125–128°C. IR spectrum, ν, cm^{-1}: 2934–2865 (–$(CH_2)_n$–), 2234 (CN), 1560, 1363 (NO_2). ^{1}H NMR spectrum, δ, ppm: 1.68–2.01 (7H, m); 2.68–2.97 (9H, m); 7.23 (0.05H, s, H-9,9' (**11**)); 7.47 (0.97H, s, H-9 (**14**)). Mass spectrum, *m*/*z* (I_{rel}, %): compound **14** – 258 $[M+H]^+$ (4), 212 $[M+H–NO_2]^+$ (100); compound **11** – 423 $[M+H]^+$ (6).

4-Nitro-1,2,3,4,5,6,7,8-octahydroacridine-4-carboxamide (15) was obtained analogously to compound **14**. Yield 10%. Colorless powder. Mp 185–188°C (MeOH). IR spectrum, ν, cm^{-1}: 3295, 3158 (NH_2), 2958–2834 (–$(CH_2)_n$–), 1707 (CO), 1541, 1370 (NO_2). ^{1}H NMR spectrum, δ, ppm: 1.49–1.82 (6H, m, 2,6,7-CH_2); 2.62–2.83 (8H, m, 1,3,5,8-CH_2); 7.32 (1H, s, H-9); 7.38 (1H, s) and 7.62 (1H, s, NH_2). Mass spectrum (EI), *m*/*z* (I_{rel}, %): 229 $[M–NO_2]^+$ (94). Mass spectrum (FAB), *m*/*z* (I_{rel}, %): 276 $[M+H]^+$ (24), 230 $[M+H–NO_2]^+$ (100). Found, %: C 60.93; H 6.14; N 15.17. $C_{14}H_{17}N_3O_3$. Calculated, %: C 61.08; H 6.22; N 15.26.

X-ray structural study of compound 4c ($C_{20}H_{19}N_5O_2$, *M* 361.40) was performed at 298 K on an Xcalibur 3 diffractometer. Crystals of compound **4c** were monoclinic, *a* 15.8978(6), *b* 12.2313(5), *c* 9.7569(5) Å; β 105.519(5)°; *V* 1828.07(15)Å^3, space group $P2_1/c$; *Z* 4; d_{calc} 1.313 g/cm^3. A total of 18841 reflections were collected ($2\theta_{max}$ 58°), including 4357 independent, R_{int} 0.036. The structure was solved directly and refined with full matrix method of least squares by F^2 using the SHELX 2013 software suite.[14] The hydrogen atom positions were determined by differential map of electron density and refined by the "rider" model with $U_{iso} = 1.2U_{eq}$ of the carrier atom. The final probability factors: wR_2 0.133 (by all independent reflections), R_1 0.060 (by 2966 reflections with $I > 2\sigma(I)$), *S* 1.07. Crystallographic data were deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1045557).

The Supplementary material is available for authorized users.

References

1. Markov, V. I.; Farat, O. K.; Varenichenko, S. A.; Velikaya, E. V. *Mendeleev Commun.* **2012**, *22*, 101.
2. Markov, V. I.; Farat, O. K.; Velikaya, E. V.; Varenichenko, S. A. *Ukr. Khim. Zh.* **2011**, *11*, 54.
3. Borsche, W.; Manteuffel, R. *Justus Liebigs Ann. Chem.* **1938**, *534*, 56.

4. Medrasi, H. Y.; Al-Sheikh, M. A.; Salaheldin, A. M. *Molecules* **2013**, *18*, 535.
5. Lamant, M. M. *C. R. Seances Acad. Sci*., *Ser. C* **1973**, *277*, 319.
6. Perronnet, J.; Girault, P. *Bull. Soc. Chim. Fr.* **1973**, 2843.
7. Shawali, A. S; Hassaneen, H. M.; Sherif, S. M. *J. Heterocycl. Chem*. **1980**, *17*, 1745.
8. Nishiwaki, T.; Kikukawa H.; Kawaji, T. *J. Fluorine Chem*. **1995**, *73*, 41.
9. Phillips, R. R. *Org. React.* **1959**, *10*, 143.
10. Butler, R. N.; Johnston S. M. *J. Chem. Soc.*, *Perkin Trans. 1* **1984**, 2109.
11. Zefirov, Yu. V.; Zorkiy, P. M. *Usp. Khim.* **1989**, *58*, 713.
12. Rüchardt, C.; Merz, E. *Tetrahedron Lett.* **1964**, *36*, 2431.
13. Varenichenko, S. A.; Farat, O. K.; Markov, V. I. *Chem. Heterocycl. Compd*. **2015**, *50*, 1602. [*Khim. Geterotsikl. Soedin.*, **2014**, 1743.]
14. Sheldrick, G. *Acta Crystallogr.*, *Sect. A: Found. Crystallogr.* **2008**, *A64*, 112.