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Chemosensor Activity of 2-(Anthracen-9-yl)-Substituted Imidazolidines and Hexahydropyrimidines

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Abstract—A number of 2-(anthracen-9-yl)-substituted imidazolidines and hexahydropyrimidines were synthesized by reaction of *N*,*N*′-bis[aryl(hetaryl)methyl]ethylene-1,2-diamines and *N*,*N*′-bis[aryl(hetaryl)methyl]-propane-1,3-diamines with anthracene-9-carbaldehyde. The obtained compounds showed chemosensor activity toward Cd^{2+}, Cu^{2+}, and Hg^{2+} ions.

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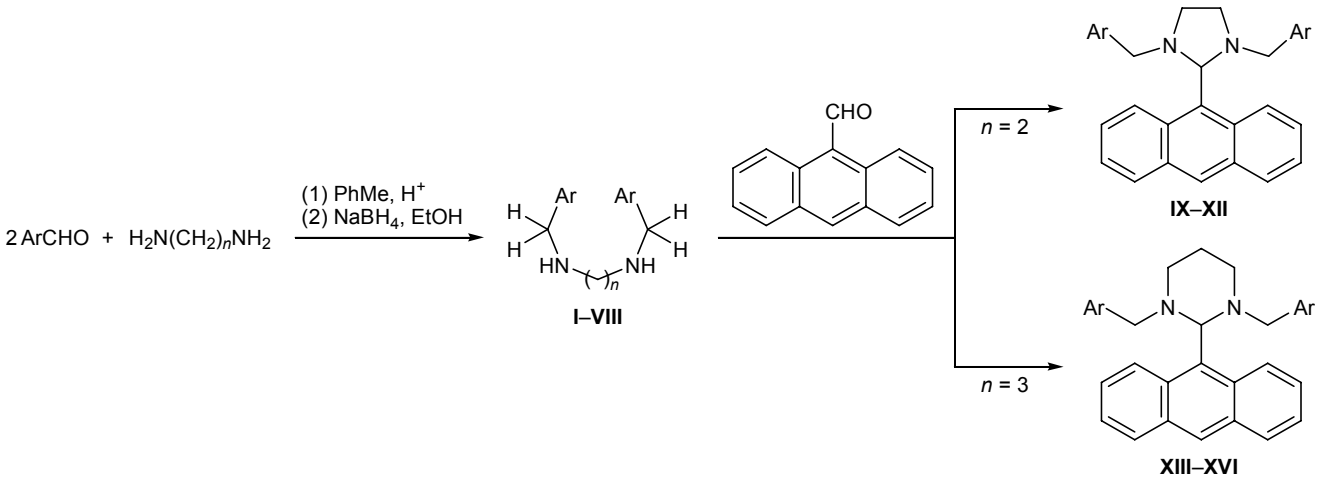
Cyclic aminals containing a saturated five-membered (imidazolidines) or six-membered ring (hexahydropyrimidines) have found diverse applications due to broad spectrum of their biological and physicochemical properties. Hydrogenated imidazole and pyrimidine derivatives exhibit anti-inflammatory and analgesic activity [1–3], act as muscarine receptors [4], and show antiparasitic and antibacterial properties [5, 6]. Coordination compounds based on imidazolidines possess both ferromagnetic and antiferromagnetic properties [7, 8]. 1,2,3-Trisubstituted imidazolidines and hexahydropyrimidines can be used in the synthesis of ion-active structures [9], as well as effective fluorescent sensors for H^+, Zn^{2+}, and Hg^{2+} cations [10] and anions [11] due to their strong complexing power.

Among 2-(anthracen-9-yl)imidazolidines, we previously found highly efficient chemosensors for Cu^{2+} and Hg^{2+} cations [12]. With a view to obtain new fluorogenic derivatives of this class of compounds, an attempt was made to extend their number via introduction of substituents into positions *1* and *3* of the heterocyclic fragment in 2-(anthracen-9-yl)-substituted imidazolidine and hexahydropyrimidine.

1,2,3-Substituted cyclic aminals are generally synthesized by reaction of the corresponding *N*,*N*′-disub-

Scheme 1.



I, **V**, **IX**, **XIII**, Ar = 2-MeC_6H_4; **II**, **VI**, **X**, **XIV**, Ar = 2-$MeOC_6H_4$; **III**, **VII**, **XI**, **XV**, Ar = 2-HO-4-MeC_6H_3; **IV**, **VIII**, **XII**, **XVI**, Ar = pyridin-2-yl; **I**–**IV**, *n* = 2; **V**–**VIII**, *n* = 3.

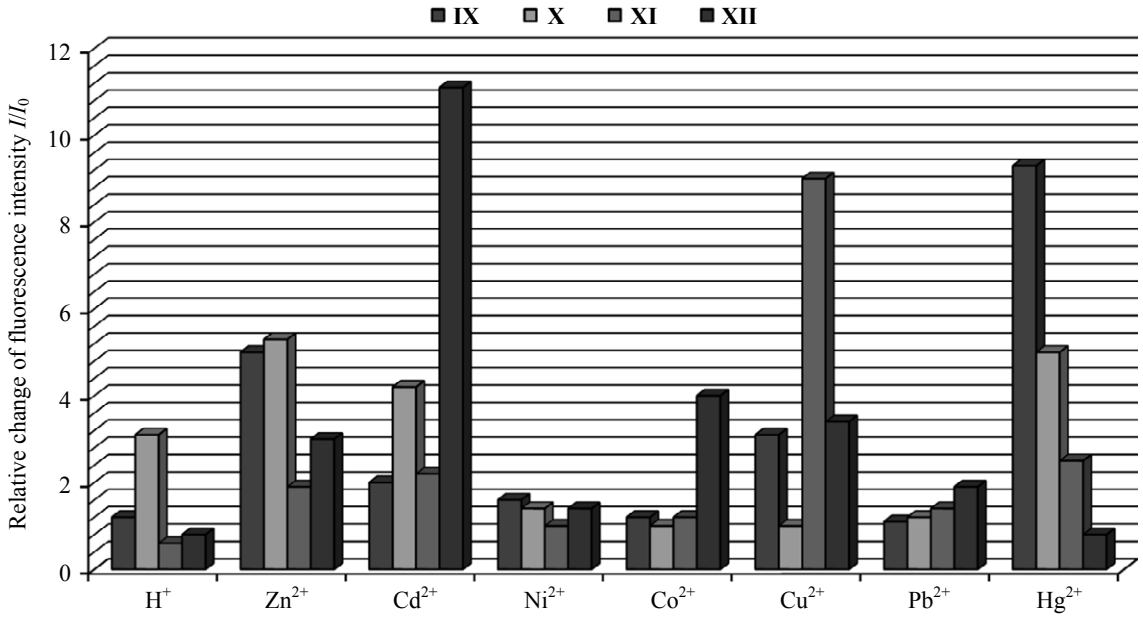


Fig. 1. Relative change of fluorescence intensity of imidazolidines **IX–XII** ($c = 5\times10^{-6}$ M) in acetonitrile upon addition of metal cations ($c = 2.5\times10^{-5}$).

stituted ethane-1,2-diamines and propane-1,3-diamines with aldehydes [13, 14]. This procedure can also be used for selective detection of a number of natural and physiologically active compounds having an aldehyde group [15]. Diarylmethyl and dihetarylmethyl derivatives of ethane-1,2-diamine (compounds **I–IV**) and propane-1,3-diamine (**V–VIII**) were prepared by reduction of the corresponding diimines [3, 13].

2-(Anthracen-9-yl)-substituted imidazolidines **IX–XII** and hexahydropyrimidines **XIII–XVI** were prepared by classical procedure from equimolar amounts of anthracene-9-carbaldehyde and the corresponding diamine **I–VIII** in toluene in the presence of acid catalyst.

The ^{1}H NMR spectra of the products characteristically contained a singlet in the region δ 5.19–5.70 ppm

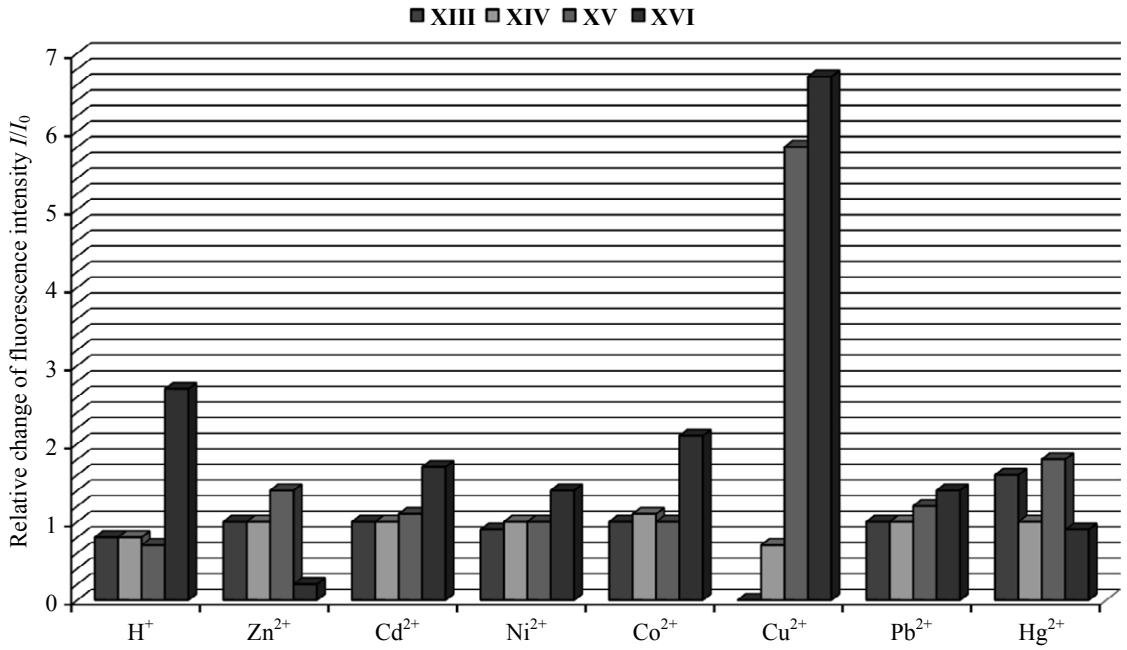


Fig. 2. Relative change of fluorescence intensity of hexahydropyrimidines **XIII–XVI** ($c = 5\times10^{-6}$ M) in acetonitrile upon addition of metal cations ($c = 2.5\times10^{-5}$).

from the 2-H proton. Conformational rigidity of the imidazolidine ring is responsible for nonequivalence of methylene protons in the heteroring, as well as in the benzyl fragments. Increase in the size of the heteroring in going to hexahydropyrimidine derivatives is accompanied by considerable complication of the spectral pattern and overlap of signals in the ^{1}H NMR spectra as a result of additional conformational distortions of the heterocyclic fragment. Signals from the 1-H and 8-H protons in the anthracene fragment were displaced appreciably downfield (by 0.5–2.0 ppm) due to interaction with the aryl(hetaryl)methyl substituents in positions *1* and *3* of the heteroring, and they appeared as two broadened singlets (imidazolidine derivatives) or doublets with a coupling constant *J* of 9.2–9.8 Hz (hexahydropyrimidines).

All compounds **IX**–**XVI** showed weak fluorescence (λ_{max} 402–450 nm) arising from specific electronic effects [16]. However, only compounds **X** and **XII** displayed typical anthracene-like fluorescence pattern (three bands, λ_{max} 402 nm), whereas fluorescence of the other compounds was characterized by a single maximum at λ_{max} 420–450 nm.

Chemosensor activity of compounds **IX**–**XVI** in solution ($c = 5\times10^{-6}$ M) was studied by comparing their fluorescence spectra before and after addition of the corresponding cations (H^+, Zn^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Pb^{2+}, Hg^{2+}; Fig. 1). As reported previously for structurally related compounds [12], the most appreciable variation of fluorescence intensity of imidazolidines **IX**–**XI** was induced by addition of Cu^{2+} and Hg^{2+} ions; simultaneously, the sensitivity to Zn^{2+} and Cd^{2+} cations increased. Bis(pyridylmethyl) derivative **XII** turned out to be more selective for Cd^{2+}. Addition of cadmium acetate to a solution of **XII** resulted in 11-fold increase of the fluorescence intensity (Fig. 1) and blue shift of the fluorescence maximum by 26 nm, indicating effective chelation of cadmium(II) ions.

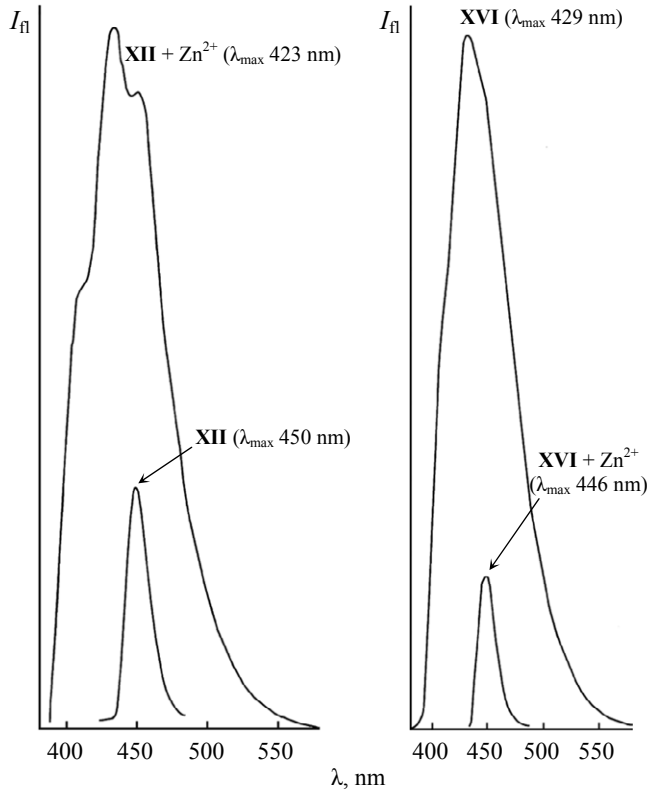


Fig. 3. Fluorescence spectra of aminals **XII** and **XVI** before and after complex formation with Zn^{2+} ions.

Increase in the size of the heteroring and hence increase in conformational mobility leads to enhanced selectivity of compounds **XIII**, **XV**, and **XVI** for copper(II) ions. However, addition of copper(II) acetate to hexahydropyrimidines **XV** and **XVI** raises the fluorescence intensity (I/I_0) by a factor of 6–7, whereas complete fluorescence quenching is observed for compound **XIII** (Fig. 2).

Differences in the sensing activities and their mechanisms between the five- and six-membered derivatives were observed most clearly in the reactions of compounds **XII** and **XVI** with Zn^{2+} cations (Fig. 3). Imidazolidine derivative **XII** shows quite weak fluorescence, which is not typical of anthracen-9-yl-substituted compounds (λ_{max} 450 nm). This is likely to be related to intramolecular photoinduced charge transfer (PCT) between the fluorophore and receptor [16, 17]. Complex formation with Zn^{2+} ions partly restores anthracene-like fluorescence spectrum (λ_{max} 423 nm) and simultaneously increases the fluorescence intensity by a factor of ~3. Obviously, the behavior of hexahydropyrimidine derivative **XVI** is determined by reverse photoinduced electron transfer (PET). In the presence of zinc(II) acetate fluorescence quenching is observed ($I^{446}/I_0^{429} = 0.25$), and the fluorescence maximum shifts by 17 nm toward longer wavelengths.

To conclude, this study on the spectral parameters and complexing power of new imidazolidine and hexahydropyrimidine derivatives containing an anthracene fragment revealed high chemosensor activity of some compounds toward heavy metal cations, such as Cd^{2+}, Cu^{2+}, and Hg^{2+}.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian Unity 300 spectrometer (300 MHz) from solutions in $CDCl_3$ or DMSO-d_6 using the residual proton signals

of the solvent as reference ($CHCl_3$, δ 7.25 ppm; DMSO-d_5, δ 2.50 ppm). The electronic absorption spectra were measured on a Varian Cary 100 spectrophotometer, and the luminescence spectra were recorded on Hitachi 650-60 and Varian Eclipse spectrofluorimeters from solutions in acetonitrile ($c = 5\times10^{-6}$ M). The IR spectra were obtained on a Specord 75IR instrument. The melting points were determined in glass capillaries using a PTP (M) melting point apparatus. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using $CHCl_3$ as eluent; spots were visualized by treatment with iodine vapor in a moist chamber.

Initial *N*,*N*′-bis(arylmethyl)ethane-1,2-diamines and *N*,*N*′-bis(arylmethyl)propane-1,3-diamines **I**–**VIII** were synthesized according to the procedures described in [13–15].

Imidazolidines IX–XII and hexahydropyrimidines XIII–XVI (*general procedure*). A solution of 3.5 mmol of the corresponding *N*,*N*′-disubstituted ethane-1,2-diamine **I**–**IV** or propane-1,3-diamine **V**–**VIII** and 3 mmol of anthracene-9-carbaldehyde in 10 ml of toluene was heated for 2 h in the presence of acetic acid as catalyst. The mixture was evaporated on a rotary evaporator, the residue was cooled, and the precipitate was filtered off, washed with cold methanol, dried in air, and recrystallized from appropriate solvent.

2-(Anthracen-9-yl)-1,3-bis(2-methylbenzyl)imidazolidine (IX). Yield 87%, mp 184–186°C (from MeCN). IR spectrum, ν, cm^{-1}: 1465, 1380. ^1H NMR spectrum, δ, ppm: 2.43 s (6H, CH_3), 2.55–2.64 q (2H, CH_2CH_2), 3.35 d (2H, CH_2, *J* = 13.0 Hz), 3.30–3.40 q (2H, CH_2CH_2), 3.70 d (2H, CH_2, *J* = 12.0 Hz), 5.58 s (1H, CH), 7.05–7.78 m (12H, H_{arom}), 8.10 d (2H, 4-H, 5-H, *J* = 8.6 Hz), 8.50 s (1H, 10-H), 8.86 br.s (1H, 1-H), 9.91 br.s (1H, 8-H). Fluorescence spectrum: λ_{max} 431 nm. Found, %: C 86.73; H 7.10; N 6.17. $C_{33}H_{32}N_2$. Calculated, %: C 86.80; H 7.06; N 6.14.

2-(Anthracen-9-yl)-1,3-bis(2-methoxybenzyl)imidazolidine (X). Yield 90%, mp 272–273°C (from diethylene glycol dimethyl ether). IR spectrum, ν, cm^{-1}: 1590, 1485, 1385. ^1H NMR spectrum, δ, ppm: 2.57–2.76 m (4H, CH_2CH_2), 3.43 s (6H, CH_3), 3.50–3.64 m (4H, CH_2), 5.64 s (1H, CH), 6.62–8.14 m (14H, H_{arom}), 8.58 s (1H, 10-H), 8.80 br.s (1H, 1-H), 9.70 br.s (1H, 8-H). Fluorescence spectrum: λ_{max} 440 nm. Found, %: C 81.20; H 6.67; N 5.65. $C_{33}H_{32}N_2O_2$. Calculated, %: C 81.12; H 6.60; N 5.73.

2-(Anthracen-9-yl)-1,3-bis(2-hydroxy-4-methylbenzyl)imidazolidine (XI). Yield 85%, mp 211–212°C (from xylene). IR spectrum, ν, cm^{-1}: 3387, 1595, 1480, 1387. ^1H NMR spectrum, δ, ppm: 2.31 s (6H, CH_3), 2.77–2.82 q (2H, CH_2CH_2), 3.48 d (2H, CH_2, *J* = 13.5 Hz), 3.50–3.60 q (2H, CH_2CH_2), 3.96 d (2H, CH_2, *J* = 13.1 Hz), 5.51 s (1H, CH), 6.71–8.00 m (12H, H_{arom}), 8.44 s (1H, 10-H), 8.52 d (1H, 1-H, *J* = 9.2 Hz), 9.14 d (1H, 8-H, *J* = 9.2 Hz), 9.87 s (2H, OH). Fluorescence spectrum: λ_{max} 420 nm. Found, %: C 81.18; H 6.65; N 5.70. $C_{33}H_{32}N_2O_2$. Calculated, %: C 81.12; H 6.60; N 5.73.

2-(Anthracen-9-yl)-1,3-bis(pyridin-2-ylmethyl)imidazolidine (XII). Yield 78%, mp 222–223°C (from butan-1-ol). IR spectrum, ν, cm^{-1}: 1595, 1465, 1385. ^1H NMR spectrum, δ, ppm: 2.75–2.83 q and 3.51–3.59 q (2H each, CH_2CH_2), 3.62 d (2H, CH_2, *J* = 12.1 Hz), 3.82 d (2H, CH_2, *J* = 12.5 Hz), 5.70 s (1H, CH), 6.83–8.45 m (15H, H_{arom}), 8.73 br.s (1H, 1-H), 9.76 br.s (1H, 8-H). Fluorescence spectrum: λ_{max} 450 nm. Found, %: C 81.00; H 6.04; N 12.96. $C_{29}H_{26}N_4$. Calculated, %: C 80.90; H 6.09; N 13.01.

2-(Anthracen-9-yl)-1,3-bis(2-methylbenzyl)hexahydropyrimidine (XIII). Yield 70% (from butan-1-ol), mp 180–181°C. IR spectrum, ν, cm^{-1}: 1450, 1380. ^1H NMR spectrum, δ, ppm: 1.50–2.38 m (10H, CH_2, CH_3), 2.63–3.30 m (6H, CH_2), 5.19 s (1H, CH), 6.74–8.50 m (15H, H_{arom}), 8.65 d (1H, 1-H, *J* = 9.2 Hz), 10.15 d (1H, 8-H, *J* = 9.2 Hz). Fluorescence spectrum: λ_{max} 402 nm. Found, %: C 86.69; H 7.31; N 6.00. $C_{34}H_{34}N_2$. Calculated, %: C 86.77; H 7.28; N 5.95.

2-(Anthracen-9-yl)-1,3-bis(2-methoxybenzyl)hexahydropyrimidine (XIV). Yield 81% (from xylene), mp 165–166°C. IR spectrum, ν, cm^{-1}: 1450, 1380. ^1H NMR spectrum, δ, ppm: 1.64–2.40 m (4H, CH_2), 2.87–3.55 m (12H, CH_2, CH_3), 5.31 s (1H, CH), 6.40–10.10 m (17H, H_{arom}). Fluorescence spectrum: λ_{max} 422 nm. Found, %: C 81.17; H 6.90; N 5.52. $C_{34}H_{34}N_2O_2$. Calculated, %: C 81.24; H 6.82; N 5.57.

2-(Anthracen-9-yl)-1,3-bis(2-hydroxy-4-methylbenzyl)hexahydropyrimidine (XV). Yield 74% (from butan-1-ol), mp 208–209°C. IR spectrum, ν, cm^{-1}: 3150, 1460, 1380. ^1H NMR spectrum, δ, ppm: 1.42–2.35 m (10H, CH_2, CH_3), 2.68–3.50 m (6H, CH_2), 5.20 s (1H, CH), 6.94–8.00 m (14H, H_{arom}, OH), 8.35 s (1H, 10-H), 8.80 d (1H, 1-H, *J* = 9.2 Hz), 10.20 d (1H, 8-H, *J* = 9.2 Hz). Fluorescence spectrum: λ_{max} 402 nm. Found, %: C 81.28; H 6.78; N 5.61. $C_{34}H_{34}N_2O_2$. Calculated, %: C 81.24; H 6.82; N 5.57.

2-(Anthracen-9-yl)-1,3-bis(pyridin-2-ylmethyl)hexahydropyrimidine (XVI). Yield 84%, mp 194–

195°C (from toluene). IR spectrum, ν, cm^{-1}: 1450, 1380. ^1H NMR spectrum, δ, ppm: 1.51–2.56 m (4H, CH_2), 3.04–3.57 m (6H, CH_2), 5.40 s (1H, CH), 6.83–8.44 m (15H, H_{arom}), 8.68 d (1H, 1-H, J = 9.8 Hz), 10.30 d (1H, 8-H, J = 9.8 Hz). Fluorescence spectrum: λ_{max} 429 nm. Found, %: C 80.97; H 6.40; N 12.63. $C_{30}H_{28}N_4$. Calculated, %: C 81.05; H 6.35; N 12.60.

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