1,3-Dipolar cycloaddition of *in situ* generated 2,2-dimethyl- and 2,2-dichlorodiazocyclopropanes to 3,3-dimethylcyclopropene

Yu. V. Tomilov, E. V. Shulishov, I. P. Klimenko, and O. M. Nefedov**

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: 007 (095) 135 5328. E-mail: tom@ioc.ac.ru

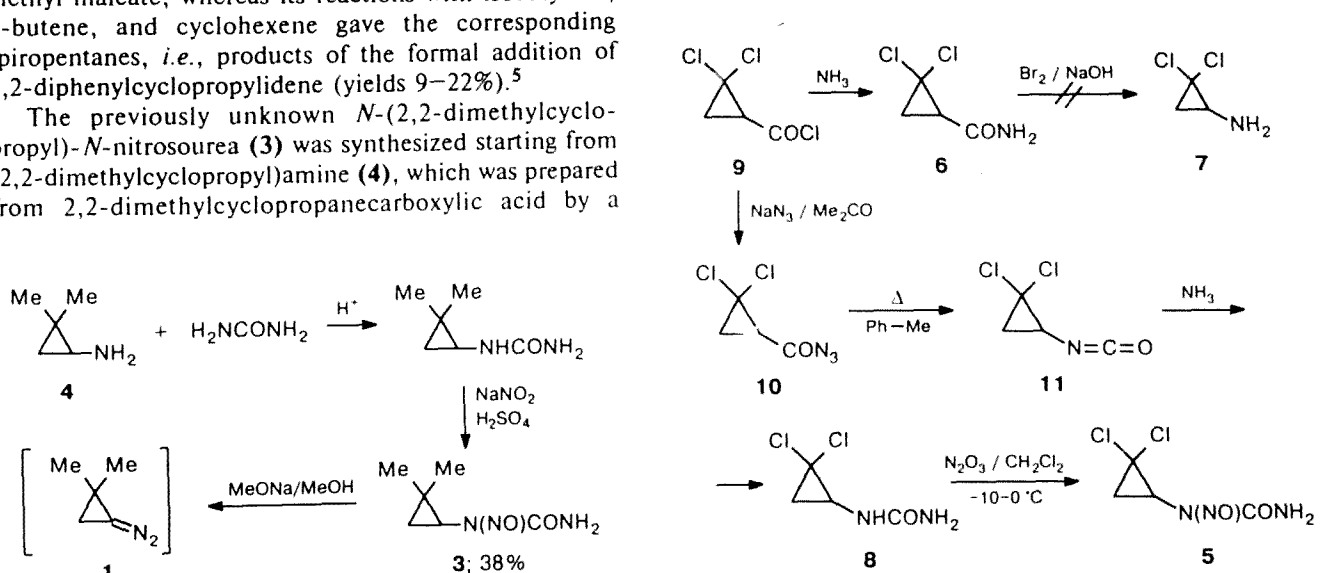
2,2-Dimethyl- and 2,2-dichlorocyclopropyl-*N*-nitrosoureas were synthesized for the first time. Under the action of MeONa/MeOH at −10°C, these compounds generate the corresponding 2,2-dimethyl- and 2,2-dichlorodiazocyclopropanes, which are readily trapped by 3,3-dimethylcyclopropene to give the products of 1,3-dipolar cycloaddition, *viz.*, isomeric substituted spiro[2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-cyclopropanes], in yields of about 70%.

Key words: spiro(1-pyrazoline-3,1′-cyclopropanes), 1,3-dipolar cycloaddition, intermediates, NMR spectra.

Previously[1,2] we have shown that cyclopropenes are effective traps for diazocyclopropane generated *in situ* and that this interaction, unlike that involving methylenecyclopropanes,[3,4] occurs exclusively as 1,3-dipolar cycloaddition to yield the corresponding 1-pyrazolines. To continue our studies dealing with the reactions of diazocyclopropanes with unsaturated compounds, we studied the interaction of 2,2-dimethyl- **(1)** and 2,2-dichlorodiazocyclopropanes **(2)**, generated *in situ* from the corresponding *N*-nitroso-*N*-cyclopropylureas, with 3,3-dimethylcyclopropene, which is used as an active dipolarophile. To the best of our knowledge, only one example of the generation and capture of a substituted diazocyclopropane, *viz.*, 2,2-diphenyldiazocyclopropane, has been reported. This compound could be converted into the corresponding spirocyclopropane-containing pyrazoline (yield 47%) only by the reaction with diethyl maleate, whereas its reactions with isobutylene, 1-butene, and cyclohexene gave the corresponding spiropentanes, *i.e.*, products of the formal addition of 2,2-diphenylcyclopropylidene (yields 9–22%).[5]

The previously unknown *N*-(2,2-dimethylcyclopropyl)-*N*-nitrosourea **(3)** was synthesized starting from (2,2-dimethylcyclopropyl)amine **(4)**, which was prepared from 2,2-dimethylcyclopropanecarboxylic acid by a known procedure.[6] The hydrochloride of amine **4** was heated with an aqueous solution of urea to give (2,2-dimethylcyclopropyl)urea, which was then nitrosated at 5–7 °C according to a procedure similar to that reported for the preparation of unsubstituted *N*-nitroso-*N*-cyclopropylurea.[7]

Synthesis of *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosourea **(5)**, which has also not been described in the literature, proved to be a more complicated problem; 2,2-dichlorocyclopropanecarboxamide **(6)**[8] did not convert into the desired (2,2-dichlorocyclopropyl)amine **(7)** under the conditions of the Hofmann rearrangement, and attempts to prepare this amine from 2,2-dichlorocyclopropanecarboxylic and hydrazoic acids in $CHCl_3$ by the Schmidt reaction led only to strong resinification of the reaction mixtures. The attempt to obtain methyl-*N*-(2,2-dichlorocyclopropyl)urethane by the reaction of



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amide **6** with bromine in methanol in the presence of MeONa also failed.

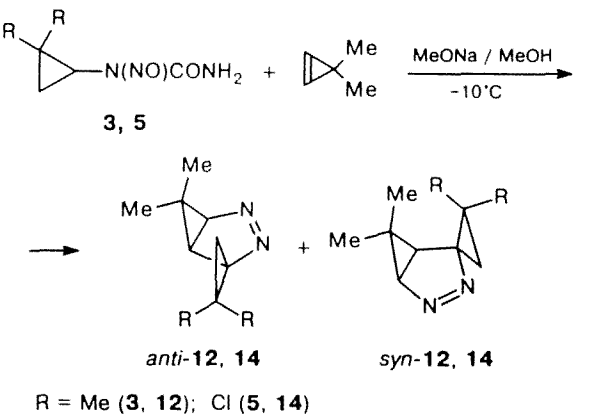
Nevertheless, we were able to synthesize *N*-(2,2-dichlorocyclopropyl)urea **(8)** without preparating amine **7**. For this purpose, 2,2-dichlorocyclopropanecarboxylic acid chloride **(9)**[8] was converted into the corresponding acylazide **10** by reacting it with NaN_3 under standard conditions; gentle heating of compound **10** without isolation in toluene (Curtius rearrangement) gave (2,2-dichlorocyclopropyl) isocyanate **(11)**, stable in an individual state, in a yield of ~68%.

Isocyanate **11** smoothly reacts with ammonia to give *N*-(2,2-dichlorocyclopropyl)urea **(8)** in a good yield. The resulting compound is poorly soluble in cold water and is readily soluble in methanol.

Subsequent nitrosation of cyclopropylurea **8** was carried out by passing nitrogen oxides through a suspension of it in CH_2Cl_2 at a temperature of −10–0 °C. This afforded *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosourea **(5)** in ~40% yield as yellowish crystals; unlike cyclopropyl- and 2,2-dimethylcyclopropyl-*N*-nitrosoures, this compound is relatively unstable and easily decomposes at ~35 °C.

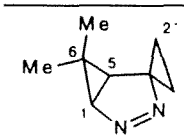
The generation and trapping of diazocyclopropanes **1** and **2** were carried out by adding sodium methoxide to a vigorously stirred solution of 3,3-dimethylcyclopropene and nitrosoureas **3** and **5** in CH_3OH at −10 °C (the molar ratio of the reactants was 1.5 : 1.5 : 1). The resulting adducts were isolated by microdistillation *in vacuo* and identified based on the data of elemental analysis and ^1H and ^{13}C NMR spectra.

For example, spiro{6,6,2′,2′-tetramethyl-2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-cyclopropane} **(12)**, obtained in ~66% yield by the decomposition of nitrosourea **3** in the presence of 3,3-dimethylcyclopropene, was a mixture of two geometrical isomers in a ratio of 2.2 : 1. The less sterically hindered *anti*-isomer, in which the methyl groups in different cyclopropane fragments are most distant from each other, apparently predominates in the mixture. The signals in the ^1H and ^{13}C NMR spectra of compound **12** were assigned by analogy with the data for 6,6-dimethylspiro{2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-cyclopropane}[1] **(13)** (Tables 1 and 2); the signals for the *exo*- and *endo*-methyl groups at C(6) were assigned according to the published data.[9,10]



R = Me (**3**, **12**); Cl (**5**, **14**)

Table 1. ^1H NMR spectra of spiro{2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-cyclopropanes)} **12** and **14** ($CDCl_3$, δ, *J*/Hz)*

Compound	H(1)	H(5)	$J_{1,5}$	H(3′) *anti*	H(3′) *syn*	J_{gem}	Me—C(6) *endo*	Me—C(6) *exo*	Me—C(2′)
 **(13)**	4.56 d	1.41 d	5.5	1.73, 1.37, 0.94 (m, 4 H)			0.64 s	1.26 s	
anti-**12**	4.41 d	1.29 d	5.0	1.72 d	0.78 d	5.0	0.54 s	1.12 s	1.39 s and 1.05 s
syn-**12**	4.37 d	1.40 d	5.0	1.65 d	1.05 d	5.0	0.50 s	1.07 s	1.41 s and 1.03 s
anti-**14**	4.85 d	1.81 d	4.7	2.75 d	2.18 d	8.1	0.89 s	1.23 s	
syn-**14**	4.83 d	2.09 d	4.6	2.68 d	2.30 d	7.6	0.64 s	1.26 s	

* For comparison, data for unsubstituted pyrazoline **13** are also presented (see Ref. 1).

Table 2. ^{13}C NMR spectra of pyrazolines **12** and **14** ($CDCl_3$), δ

Compound	C(1)	C(4)	C(5)	C(6)	C(2′)	C(3′)	Me—C(6) *endo*	Me—C(6) *exo*	Me—C(2′)
13	76.0	67.5	13.5	22.1	10.9 and 14.9		24.0 and 32.6		
anti-**12**	75.2	78.3	32.6	26.4	21.5	30.6	13.4	25.1	22.1 and 23.6
syn-**12**	74.8	76.7	29.0	25.5	20.1	25.6	12.9	23.9	20.7 and 21.7
anti-**14**	77.9	61.5	32.7	27.0	38.2	34.6	13.6	23.8	
syn-**14**	76.8	60.6	30.4	26.8	47.3	30.0	13.1	24.0	

When the reaction was carried out directly in an ampule of an NMR spectrometer (in CD_3OD), signals for several impurities were observed, along with the signals for the target product. For example, the septet at δ 4.44 and the triplet at δ 1.62 refer to 3-methylbuta-1,2-diene. When there is no excess of 3,3-dimethylcyclopropene, the integral intensities of these signals in the ^1H NMR spectrum markedly increase and become as high as ~40% of the total intensity of all signals. This result, similarly to those obtained in the experiments on the generation of unsubstituted diazocyclopropane[7] or 2,2-diphenyldiazocyclopropane,[5] indicate that there is a possibility of partial formation of 2,2-dimethylcyclopropylidene and of its isomerization into the corresponding allene.

The interaction of nitrosourea **5** with sodium methoxide under similar conditions results in the generation of 2,2-dichlorodiazocyclopropane **(2)**, which is also efficiently trapped by 3,3-dimethylcyclopropene, to give isomeric *anti*- and *sin*-spiro{6,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-(2′,2′-dichlorocyclopropanes)} **(14)** in a yield of no less than 70% and in a ratio of ~1 : 1.3. The data of the ^1H and ^{13}C NMR spectra are presented in Tables 1 and 2. A comparison of the integral intensities of the ^1H NMR signals, together with the fact that the signal for the *endo*-CH_3 group in the major isomer shifts downfield (δ 0.89) due to the deshielding effect of the closely spaced chlorine atoms in the spirocyclopropane fragment, make it possible to infer that in this case, unlike the situation with pyrazolines **12**, the *syn*-isomer predominates somewhat.

Thus, the formation of adducts **12** and **14**, which are obtained in relatively high yields, is evidence for the intermediate formation of 2,2-dimethyl- and 2,2-dichlorodiazocyclopropanes followed by their easy 1,3-dipolar cycloaddition to 3,3-dimethylcyclopropene.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 (200 and 50.3 MHz) and Bruker AM-300 (300 and 75.47 MHz) spectrometers for solutions in $CDCl_3$ and CD_3OD containing 0.1% tetramethylsilane as the internal standard. The GC/MS spectra were obtained on a Finnigan MAT INCOS-50 instrument (70 eV, a 30 m-long RSL-200 capillary column). IR spectra were measured on a Bruker IFS-113v spectrometer in thin films. 2,2-Dimethylcyclopropylamine and the chloride and amide of 2,2-dichlorocyclopropanecarboxylic acid were prepared by previously described procedures.[6,8]

***N*-(2,2-Dimethylcyclopropyl)-*N*-nitrosourea (3).** A 2*N* solution of HCl (7.5 mL) was added dropwise and then urea (4.2 g, 0.07 mol) was added with stirring to 2,2-dimethylcyclopropylamine (1.28 g, 0.015 mol). (2,2-Dimethylcyclopropylamine hydrochloride: ^1H NMR (D_2O), δ: 4.85 (br.s, $H_3N^+-H_2O$), 2.42 (br.d.d, H-1, J_{cis} = 7.6 Hz, J_{trans} = 4.0 Hz), 1.19 and 1.08 (both s, 2 CH_3), 0.84 and 0.63 (both d.d, 2 H-3, J_{gem} = 6.3 Hz); ^{13}C NMR (D_2O) δ: 35.9 (C-1), 26.4 and 20.4 (2 Me), 19.9 (C-3), 17.9 (C-2).) The resulting solution was boiled for 3 h and cooled to 5 °C. $NaNO_2$ (1.04 g, 0.015 mol) was dissolved in the solution, H_2SO_4 (0.9 g) was added dropwise with stirring, and 5 g of ice was added, while maintaining a temperature of 5–7 °C. The precipitate that formed was filtered off, washed with 3 mL of ice water, and dried in a vacuum desiccator to give 0.9 g (38%) of the product as a yellow finely crystalline solid, dec. temp. ≥85 °C. ^1H NMR (CD_3OD), δ: 4.80 (br.s, NH_2), 2.09 (dd, H-1, J_{cis} = 7.9, J_{trans} = 5.0), 1.10 and 0.70 (both s, 2 CH_3), 0.98 and 0.60 (both dd, 2 H-3, J_{gem} = 5.9). ^{13}C NMR (CD_3OD), δ: 181.3 (CO), 36.7 (C-1), 24.8 and 21.8 (2 Me), 20.9 (C-2), 20.3 (C-3). Compound **3** was used without additional purification.

An attempt to prepare 2,2-dichlorocyclopropylamine. Potassium hydroxide (4.4 g, 0.08 mol) and 30 mL of water were placed in a flask equipped with a stirrer and cooled to 0 °C. Bromine (0.8 mL, 0.015 mol) and then 2,2-dichlorocyclopropanecarboxamide **(6)** (2 g, 0.013 mol) were added. The mixture was stirred for 25 min at 0° C and kept for 3 days at 15 °C. The color due to bromine persisted, and the ^1H NMR spectrum of the organic layer showed that it contained the starting amide **6**. When the temperature of the reaction mixture was increased to 60 °C, the amount of the starting amide **6** in the mixture decreased but 2,2-dichlorocyclopropylamine **(7)** was totally lacking.

An attempt to prepare methyl 2,2-dichlorocyclopropylcarbamate. A solution containing MeOH (40 mL), MeONa (1.4 g, 0.026 mol), and amide **6** (2.0 g, 0.013 mol) were placed in a flask equipped with a stirrer and a reflux condenser; bromine (0.7 mL, 0.013 mol) was added, and the mixture was stirred for 45 min. Then 2 mL of the mixture was withdrawn, concentrated on a rotary evaporator, and its ^1H NMR spectrum in CD_3OD was recorded. (The spectrum corresponded to the starting amide.) The remaining reaction mixture was boiled for 15 min and acidified to pH = 5; the solvent was evaporated, and the residual liquid was diluted with ether. The ethereal layer was washed twice with water, the layers were separated, and samples for ^1H NMR spectroscopy were prepared. No methyl 2,2-dichlorocyclopropylcarbamate was detected in any of the fractions.

2,2-Dichlorocyclopropyl isocyanate (11). At 0 °C, a solution of NaN_3 (2.75 g, 0.04 mol) in 7.7 mL of H_2O was added with stirring to a solution of 2,2-dichlorocyclopropanecarboxylic acid chloride **(9)** (6.15 g, 0.035 mol) in 45 mL of anhydrous acetone, the mixture was stirred for 30 min, and then 200 mL of H_2O was added. The product was extracted with benzene (20 mL) and dried with anhydrous Na_2SO_4. A small portion of the solution was concentrated *in vacuo* at a temperature of no more than 10 °C, the residue was dissolved in $CDCl_3$, and its ^1H NMR spectrum was recorded; the spectrum corresponded to the structure of the azide of 2,2-dichlorocyclopropanecarboxylic acid **(10)**. ^1H NMR ($CDCl_3$), δ: 2.48 (dd, H-1, J_{cis} = 9.5 Hz, J_{trans} = 7.6 Hz); 2.08 (t, H-3, J_{gem} = J_{trans} = 7.6 Hz); 1.88 (dd, H-3, J_{gem} = 7.6 Hz, J_{cis} = 9.5 Hz). The benzene solution of azide **10** was diluted with 45 mL of toluene, and most of the benzene was evaporated *in vacuo*. Then the solution was kept on a water bath at 90–95 °C for 1.5 h until evolution of nitrogen ceased. When the reaction was completed, the mixture was fractionated *in vacuo* to give 3.62 g (68%) of 2,2-dichlorocyclopropyl isocyanate **(11)**, b.p. 50–51° (10 Torr). ^1H NMR ($CDCl_3$), δ: 3.29 (dd, H-1, J_{cis} = 8.5 Hz, J_{trans} = 6.0 Hz); 1.87 (t, H-3, J_{gem} = J_{cis} = 8.5 Hz); 1.57 (dd, H-3, J_{trans} = 6.0 Hz, J_{gem} = 8.5 Hz). ^{13}C NMR ($CDCl_3$), δ: 128.4 (NCO); 58.8 (CCl_2); 39.2 (CH); 29.5 (CH_2). IR, ν/cm^{-1}: 2278 (NCO). MS, *m/z* (*I*(%)): 153 (0.4), 152 (0.5), 151 (0.8), 150 (1.2) M^+ and $(M-H)^+$, 118 (39) and 116 (100) $(M-Cl)^+$. Found (%): C, 31.85; H, 2.03; N, 9.30; Cl, 46.38. $C_4H_3Cl_2NO$. Calculated (%): C, 31.63; H, 1.99; N, 9.22; Cl, 46.65.

***N*-(2,2-Dichlorocyclopropyl)urea (8)**. An excess of dry NH_3 was passed through a solution of isocyanate **11** (2 g, 0.013 mol) in 40 mL of ether. The precipitate that formed was filtered off. The filtrate was concentrated to 1/4 its initial volume, and the additional precipitate thus formed was combined with the first portion. This gave 2.05 g (92%) of *N*-(2,2-dichlorocyclopropyl)urea as small colorless crystals, which start to decompose slowly at 75° C. ^{1}H NMR (CD_3OD), δ: 4.75 (br.s, 3 H, NH, NH_2); 3.32 (dd, H-1, J_{trans} = 6.0 Hz, J_{cis} = 9.5 Hz); 1.87 (dd, H-3, J_{cis} = 9.5 Hz, J_{gem} = 8.0 Hz); 1.48 (dd, 1H, J_{trans} = 6.0 Hz, J_{gem} = 8.0 Hz). Found (%): C, 27.75; H, 3.43; N, 16.30; Cl, 41.25. $C_4H_6Cl_2N_2O$. Calculated (%): C, 28.43; H, 3.58; N, 16.58; Cl, 41.95.

***N*-Nitroso-*N*-(2,2-dichlorocyclopropyl)urea (5)**. An eightfold excess of N_2O_3, prepared from sodium nitrite and concentrated hydrochloric acid, was passed at −10 °C through a mixture of *N*-(2,2-dichlorocyclopropyl)urea (1.2 g, 7 mmol) and CH_2Cl_2 (55 mL); then argon was passed through the mixture for 40 min. The precipitate was filtered off, the filtrate was evaporated *in vacuo* at 10 °C to 1/3 its initial volume, and the additional precipitate thus formed was filtered off, washed with ice water, and dried in a vacuum desiccator at a temperature not exceeding 10 °C to give 0.55 g (~40%) of *N*-nitroso-*N*-(2,2-dichlorocyclopropyl)urea as a yellowish solid, decomp. temp. ~35 °C. ^{1}H NMR (CD_3OD), δ: 4.8 (br.s, NH_2), 3.25 (dd, H(1), J_{cis} = 9.5 Hz, J_{trans} = 7.0 Hz); 2.30 (t, *trans*-H(3), J_{cis} = 9.5 Hz, J_{gem} = 9.5 Hz); 2.10 (dd, *cis*-H(3), J_{trans} = 7.0 Hz, J_{gem} = 9.5 Hz). Compound **5** was used further without additional purification.

Spiro{6,6,2′,2′-tetramethyl-2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-(cyclopropane)} (12). At −10 °C, 3,3-dimethylcyclopropene (0.20 g, 3 mmol) and then, with intense stirring, sodium methoxide (0.16 g, 3 mmol) were added to a solution of *N*-nitroso-*N*-(2,2-dimethylcyclopropyl)urea **(3)** (0.32 g, 2 mmol) in 3 mL of CH_3OH. The yellowish solution gradually became almost colorless. The mixture was poured into ice and extracted with ether. Vacuum microdistillation (at a temperature of the bath of 83–86 °C (0.5 Torr)) gave 0.22 g (~66%) of a slightly yellowish liquid, which was a mixture of two isomeric 1-pyrazolines **12** in a ratio of 2.2 : 1. The ^{1}H and ^{13}C NMR spectra of these compounds are presented in Tables 1 and 2. Found (%): C, 72.97; H, 9.94; N, 17.01. $C_{10}H_{16}N_2$. Calculated (%): C, 73.13; H, 9.82; N, 17.05.

Spiro{6,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene-4,1′-(2′,2′-dichlorocyclopropane)} (14). This procedure was similar to the previous one. The reaction between *N*-nitroso-*N*-(2,2-dichlorocyclopropyl)urea **(5)** (0.30 g, 1.5 mmol), 3,3-dimethylcyclopropene (0.15 g, 2.2 mmol), and sodium methoxide (0.12 g, 2.2 mmol) followed by filtration through a thin silica gel layer and removal of the solvents afforded 0.22 g (~70%) of a yellowish liquid, which was a mixture of two isomeric 1-pyrazolines **14** in a ratio of 1.3 : 1. After vacuum microdistillation (at a temperature of the bath of 93–98 °C (0.2 Torr)), the content of the minor isomer (apparently *anti*-**14**) markedly decreased. The ^{1}H and ^{13}C NMR spectra are presented in Tables 1 and 2. Found (%): C, 46.56; H, 4.98; Cl, 34.08. $C_8H_{10}Cl_2N_2$. Calculated (%): C, 46.85; H, 4.91; Cl, 34.57.

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