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Pathways of decomposition of *N*-cyclopropyl-*N*-nitrosoureas in methanol

I. P. Klimenko and Yu. V. Tomilov*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (095) 135 6390. E-mail: tom@ioc.ac.ru

Decomposition of a series of *N*-cyclopropyl-*N*-nitrosoureas (CNU) in CD_3OD was studied. These decompose much more rapidly than *N*-methyl-*N*-nitrosourea, one of the decomposition pathways being denitrosation, which is atypical of alkylnitrosoureas under the reaction conditions used. The nature of substituents in the cyclopropane ring has a great effect on the stability of CNU and the product ratio. In the presence of H_2SO_4, decomposition occurs much more rapidly. Possible pathways of the formation of the major decomposition products of CNU are proposed based on the experimental data.

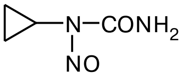
Key words: cyclopropylnitrosoureas, denitrosation, cyclopropanediazonium ion, reaction mechanisms, NMR spectra.

In our recent studies[1] aimed at investigating the reactivities of diazocyclopropanes and cyclopropanediazonium ions containing various substituents in the cyclopropane ring, we faced the problem of synthesizing *N*-cyclopropyl-*N*-nitrosoureas (CNU) as the sources for the generation of these species. It appeared that some of these nitroso compounds decompose during storage in protic solvents. One of decomposition pathways involves denitrosation giving rise to the corresponding *N*-cyclopropylurea. Investigations into decomposition pathways of nitrosoureas are topical, because this class of compounds can serve as both NO donors with a broad spectrum of biological activities[2] and alkylating agents (sources of diazonium ions), which either induce or, to the contrary, inhibit cancer cell growth.[3] It is important to know possible mechanisms of decomposition of nitrosoureas and reveal the factors favorable for a particular reaction pathway in order to elucidate their role *in vivo*. It should be noted that denitrosation of *N*-alkyl-*N*-nitrosoureas containing one alkyl substituent at the N atom, unlike that of di- and trialkyl-substituted *N*-nitrosoureas, is poorly studied so far. There are, actually, only two publications dealing with this reaction. *N*-Methyl-*N*-nitrosourea (MNU) was demonstrated[4] to undergo denitrosation in aqueous solutions at pH < 1. Denitrosation of *N*-ethyl- and *N*-methyl-*N*-nitrosoureas in the presence of piperidine or morpholine[5] was accompanied by the formation of *N*-nitrosoamines.

The available fragmentary data on decomposition of CNU in protic solvents stimulated us to perform systematic investigations of these processes. In the present study, we performed solvolysis of six *N*-cyclopropyl-*N*-nitrosoureas in methanol and examined the influence of the substituents in the cyclopropane ring on the rate of decomposition of these compounds and the product ratio. It should be noted that a thorough kinetic investigation was beyond the scope of the present study, because our current aim was to compare the stabilities of various nitrosoureas and investigate their decomposition pathways.

Results and Discussion

We studied *N*-cyclopropyl-*N*-nitrosourea (**1**), *gem*-disubstituted CNU containing substituents of various nature, *viz.*, *N*-(2,2-dichlorocyclopropyl)- (**2**), *N*-(2,2-dimethylcyclopropyl)- (**3**), *N*-(spiropentyl)- (**4**), and



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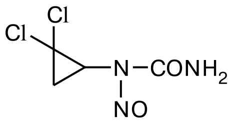

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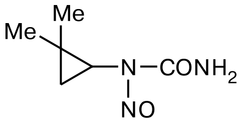

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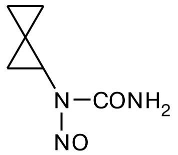

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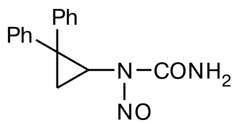

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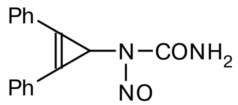

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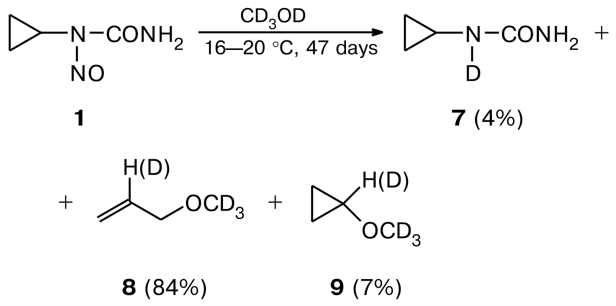
N-(2,2-diphenylcyclopropyl)-*N*-nitrosourea (**5**), and also *N*-(2,3-diphenylcycloprop-2-enyl)-*N*-nitrosourea (**6**).

Solutions of CNU with the same concentrations (0.125 mol L^{-1}) were prepared in CD_3OD. The reactions were monitored by ^1H NMR spectroscopy. The percentages of the starting CNU and reaction products were determined by comparing the integral intensities of the corresponding signals in the ^1H NMR spectra with that of the signal for the residual proton of deuteriomethanol (CHD_2OD) used as the standard. Solutions of nitrosoureas were kept in the dark at 16—20 °C.

Complete decomposition of cyclopropylnitrosourea **1** in CD_3OD (Scheme 1) took 47 days. After 4 days, allyl ether **8** (~20% yield) and trace amounts of compounds **7** and **9** were detected in the reaction mixture. The half-life ($t_{1/2}$) of nitroso compound **1** is ~14 days. Compounds **7—9** were synchronously accumulated in the reaction medium and their total yield reached ~95% by the end of the reaction. The reaction mixture contained also unidentified minor products.

Scheme 1



1

7 (4%)

8 (84%) **9** (7%)

It is noteworthy that this reaction affords *N*-cyclopropylurea (**7**) in small, although noticeable, amounts. Earlier, it has been noted[6] that, in aqueous solutions at pH > 2, MNU undergoes only hydrolysis to give methanol. More recently,[5] it has been demonstrated that MNU partly loses the nitroso group at pH 3.3 in the presence of a substrate trapping the NO^+ cation. Nitrosourea **1**, unlike MNU, undergoes denitrosation under neutral conditions in the absence of an efficient acceptor of the NO^+ cation, whereas MNU is stable in anhydrous MeOH at 25 °C for several weeks.[6] Therefore, nitrosourea **1** is a much more labile compound in protic solvents.

Interestingly, ethers **8** and **9**, which are the major methanolysis products of urea **1**, contain deuterium not only in the methoxy group but also at position 2 of the allyl ether and position 1 of the cyclopropyl ether, as is evident from the ^1H NMR spectra. The NMR spectrum recorded at 300 MHz after complete decomposition of nitrosourea **1** showed four multiplets at δ 5.89 (H(2)), 5.26 (H(3)), 5.16 (H(3)), and 3.92 (H(1)) characteristic of the allylic system. The integral intensity ratio of the corresponding signals was 0.4 : 1 : 1 : 2.* An increase in the operating frequency of the NMR spectrometer to 500 MHz demonstrated that the multiplets at δ 5.26, 5.16, and 3.92 result from overlap of the signals of 1-(trideuteriomethoxy)prop-2-ene (**8**), whose spectrum in CD_3OD has been described earlier,[8] and its isotopomer, *viz*., 2-deuterio-1-(trideuteriomethoxy)prop-2-ene (**8**-d). The signals of the latter have somewhat lower chemical shifts (the deuterium isotope effect[7]) and a characteristic multiplicity (see Experimental), which confirms the presence of the D atom at position 2. The ratio of the coupling constants $J_{H(3),H(2)}$ in the spectrum of compound **8** to the coupling constants $J_{H(3),D(2)}$ in the spectrum of compound **8**-d corresponds to the theoretical value $J_{H,H}/J_{H,D} = 6.5$ (Ref. 7).

In the ^1H NMR spectrum of ether **9**, the signal for the methine proton of the cyclopropane fragment at δ 3.24 appears as a characteristic triplet of triplets with J_{cis} = 6.0 Hz and J_{trans} = 3.0 Hz, and a complex multiplet is observed at high field (δ 0.43—0.51) corresponding to the other four protons of the cyclopropane ring, which is in good agreement with the spectrum of methoxycyclopropane described earlier.[9] However, the integral intensity ratio of these multiplets is ~0.4 : 4, which suggests partial incorporation of the D atoms at position 1 of the cyclopropane ring.

It should be emphasized that the formation of a mixture of allyl ether **8** and cyclopropyl ether **9** (including partially deuterated) upon decomposition of nitrosourea **1** is not surprising and has been noted earlier.[10] However, decomposition of CNU was carried out, as a rule, using basic reagents (MeONa, NaOH, $NaHCO_3$, *etc*.) or strong nucleophiles (LiN_3, NaI). The presence of deuterium in solvolysis products of nitrosourea **1** is attributable[10] to the reversible transformation of the cyclopropanediazonium ion into diazocyclopropane** (Scheme 2).

These data suggest that, even in the absence of bases, the interconversion between the cyclopropanediazonium ion and diazocyclopropane proceeds more rapidly than the elimination of nitrogen from the cyclopropanediazonium ion. The fact that the degree of deuteration of allyl ether **8** is equal to the degree of deuteration of cyclopropyl ether **9** (~60%) agrees well with this scheme and indicates that the deuterium exchange precedes the cyclopropane ring opening. It should be emphasized that under these conditions, the methine proton in the starting CNU is not exchanged for deuterium, because the integral intensity ratio of the signals for the protons of the cyclopropane ring in CNU **1** at δ 2.36, 1.02, and 0.57 is 1 : 2 : 2 throughout the reaction.

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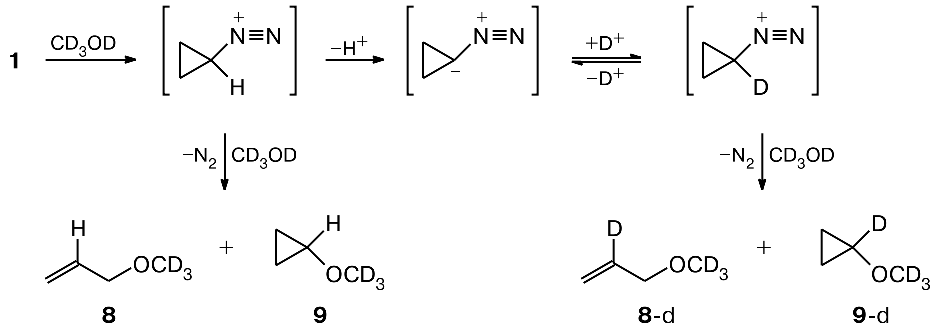
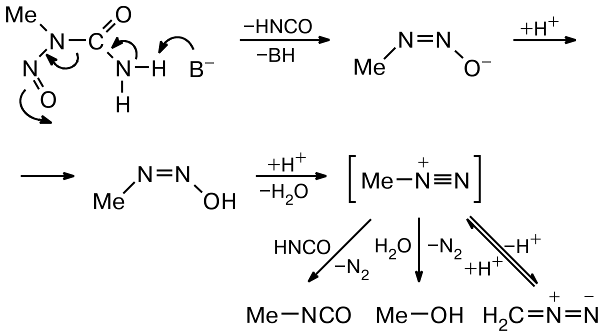
* The integration accuracy was ~4% (see, for example, Ref. 7).

** There is a large body of data on the intermediate formation and interconversions of diazocyclopropane and the cyclopropanediazonium ion (see, for example, Refs 1 and 10—12).

Scheme 2



Scheme 3



B is a base

Based on quantum-chemical calculations performed earlier,[12] it can be hypothesized that cyclopropyl methyl ether **9** is formed by the S_N2 reaction of methanol with the cyclopropanediazonium ion. The latter can also spontaneously eliminate the nitrogen molecule with simultaneous ring opening and generation of the allylic cation followed by the formation of allyl methyl ether **8**. The intermediate formation of the cyclopropyl cation is energetically unfavorable (see Ref. 12) and it is unlikely to be a transient species in this reaction.

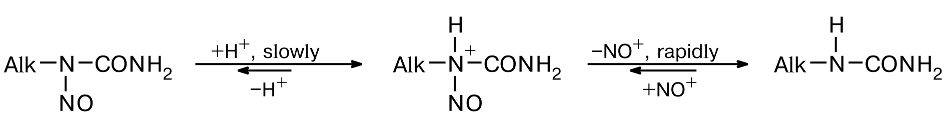
The sequence of transformations of alkylnitrosoureas giving rise to diazo compounds has long been debated.[13] A mechanism of decomposition of MNU in aqueous buffer solutions (Scheme 3) at pH varying from 6.5 to 10 was proposed.[13] It was noted that decomposition of MNU in D_2O is accompanied by the partial incorporation of the D atom in the Me group of the methanol formed in the reaction. This process occurs due to interconversions in the methanediazonium ion—diazomethane system.

In our case, it is the methoxide ion that would abstract a proton from the NH_2 group in the decomposition of nitrosourea **1** in methanol in the absence of bases, which is hardly probable. Due to a low concentration of the methoxide ions, decomposition of nitrosourea **1** is unlikely to occur at the observed rate.

In addition, if the decomposition of CNU giving rise to compounds **8** and **9** occurs by a mechanism analogous to that shown in Scheme 3, then the decomposition rate of nitrosourea in an acidified reaction medium should be lower because the concentration of species capable of acting as bases substantially decreases. However, experimental data demonstrated that the addition of catalytic amounts of H_2SO_4 noticeably accelerates decomposition of nitrosourea **1** (after 24 h, the conversion of **1** is ~52%). The reaction affords cyclopropylurea **7** and allyl methyl ether **8** as the major products in a ratio of ~1.7 : 1, whereas cyclopropyl methyl ether **9** is present in trace amounts. A substantial contribution of denitrosation upon the addition of an acid is expected because it is known[4,5] that acid catalysis facilitates denitrosation of alkylnitrosoureas (Scheme 4).

In the decomposition of nitrosourea **1** under acidic conditions, the rate of the reaction giving rise to allyl ether **8** also increases. Thus in the presence of H_2SO_4, 52% of CNU decomposes within 24 h to give cyclopropylurea **7** and allyl methyl ether **8** in a ratio of 1.7 : 1. Hence, 33% of CNU is transformed into urea **7**, and 19% of CNU decomposes to give ether **8**. When the reaction was carried out in neutral CD_3OD, an analogous degree of conversion of the nitrosourea into the allyl ether was observed only after 4 days (see above). Thus, hydrolysis of CNU yielding compounds **8** and **9** is substantially accelerated at lower pH and, consequently, the decomposition

Scheme 4



mechanism of nitrosoureas changes in the absence of bases.

We hypothesized that decomposition of nitrosoureas in the absence of bases occurs by a mechanism that involves the first step different from that proposed earlier.[13] Apparently, the electron density in the nitrosourea molecule is redistributed to form a double bond between the N atom of the NH_2 group and the carbonyl C atom, resulting in decomposition of nitrosourea to give HNCO and diazohydroxide. Obviously, a protic solvent can activate the O atoms of the carbonyl and nitroso groups of nitrosourea, thus facilitating this process (Scheme 5, path *A*). In the presence of an acid, activation of the carbonyl and nitroso groups of nitrosourea plays a greater role, which seems to be responsible for the acceleration of the reaction. An analogous scheme has been proposed earlier[14] for acid catalysis of decomposition of nitrosoamides in aqueous media.

Nitrosourea also decomposes without preliminary protonation of the O atoms (see Scheme 5, path *B*). In this case, one H atom of the NH_2 group is transferred to the oxygen atom of the nitroso group through the six-membered transition state. The transfer of the H atom and elimination of the HNCO molecule occurs both simultaneously and successively. An analogous mechanism has been proposed earlier[15] for thermal decomposition of *N*-alkyl-*N*-nitrosoureas in ethanol or benzene.

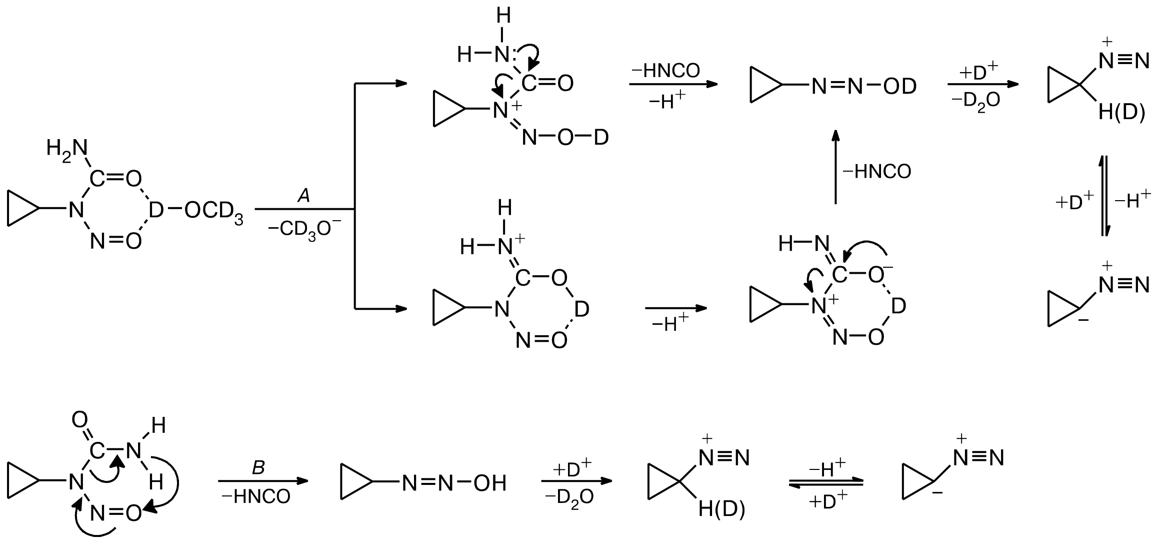
Therefore, it becomes clear that on going from acidic to basic media, decomposition of *N*-alkyl-*N*-nitrosoureas to alkoxy compounds initially slows down (in a neutral medium) and then is sharply accelerated after the addition of bases. Apparently, the mechanism of the reaction in acidic solutions differs from that in basic solutions. In a particular pH range, both reaction mechanisms operate simultaneously. It should be emphasized that the kinetic data,[13] from which the conclusion about the solvolysis mechanism of MNU was drawn, were obtained in a phosphate buffer, where the HPO_4^{2-} anion acts as a base abstracting a proton from the NH_2 group. It was correctly noted[13] that decomposition of MNU in a buffer solution occurred rather rapidly and proceeded as a first-order reaction, whereas in the absence of the phosphate buffer, the reaction proceeded much more slowly and did not follow the first-order kinetics.

The observed decomposition of nitrosourea **1** in CD_3OD in the presence of H_2SO_4 also suggests that the rate of deuterium exchange in the cyclopropanediazonium intermediate in an acidic medium is much lower than the rate of its dediazotization due to the shift of the cyclopropanediazonium ion—diazocyclopropane equilibrium toward the former. Therefore, no deuterium is incorporated into the reaction products. In the ^{1}H NMR spectrum, which was recorded after complete decomposition of nitrosourea **1**, the integral intensity ratio of the signals of the allylic system of compound **8** at δ 5.89 (H(2)), 5.26 (H(3)), 5.16 (H(3)), and 3.92 (H(1)) is ~1 : 1 : 1 : 2 compared to the ratio of 0.4 : 1 : 1 : 2 for these signals observed for the reaction in neutral CD_3OD (see Scheme 1).

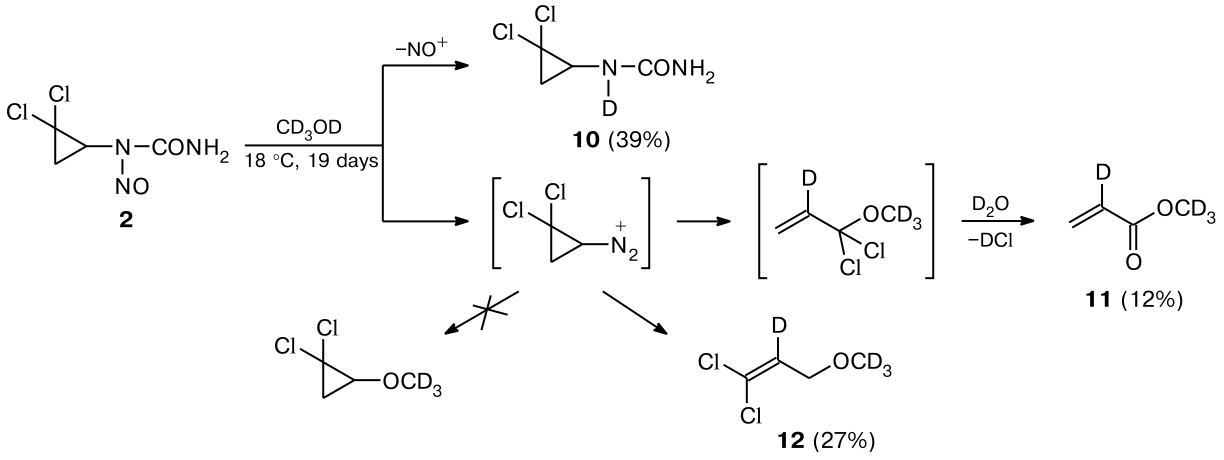
Among other CNU, *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosourea (**2**) appeared to be the most labile in CD_3OD. Its decomposition is completed (Scheme 6) in 19 days and the half-life is <5 days. Three major decomposition products, *viz*., compounds **10—12**, were identified by ^{1}H NMR spectroscopy, their ratio being virtually unchanged during the reaction.

In this case, denitrosation is pronounced, and urea **10** is the major reaction product (see Scheme 6). By analogy with decomposition of unsubstituted CNU, this reaction

Scheme 5



Scheme 6

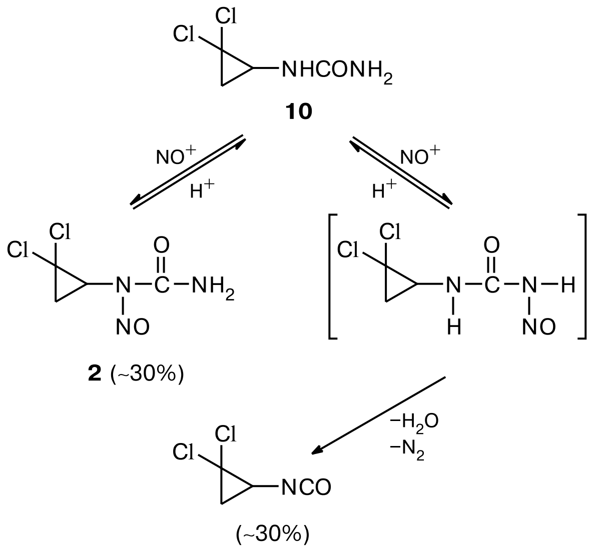


would be expected to afford three compounds assuming the involvement of the cyclopropanediazonium ion as an intermediate, *viz.*, 1,1-dichloro-2-(trideuteriomethoxy)cyclopropane, 1,1-dichloro-3-(trideuteriomethoxy)prop-1-ene, and 1,1-dichloro-1-(trideuteriomethoxy)prop-2-ene (see Scheme 6). Under these conditions, the former compound is not produced (^{1}H NMR spectroscopic data; for the spectrum of 1,1-dichloro-2-methoxycyclopropane, see Ref. 16), and the latter compound is apparently unstable and is hydrolyzed with traces of water to form acrylate **11**. The ^{1}H NMR spectra of acrylate **11** and 1,1-dichloro-2-deuterio-3-(trideuteriomethoxy)prop-1-ene (**12**) with account of the coupling constant ratio $J_{\mathrm{H,H}}/J_{\mathrm{H,D}} = 6.5$ (Ref. 7) agree well with the spectra of their nondeuterated analogs[17,18] (see Experimental).

Interestingly, the degree of deuteration at position 2 of unsaturated compounds **11** and **12** is ~100%, although pH of the solution decreases with time (due to elimination of DCl upon the formation of acrylate **11**) and reaches 2 by the end of the reaction. Recall that in the case of decomposition of nitrosourea **1** in CD_3OD, the degree of deuteration of allyl ether **8** at position 2 is ~60% (see Scheme 1), whereas the D atom at this position is absent upon decomposition in the presence of an acid. Thus, the incorporation of two Cl atoms into the cyclopropane ring leads to a considerable increase in the rate of interconversion between the cyclopropanediazonium ion and diazocyclopropane (see Scheme 2) compared to dediazotization rate. In this case, the 2,2-dichlorocyclopropanediazonium ion eliminates the proton even in an acidic medium, as opposed to the unsubstituted analog. Earlier,[1] we have suggested that the introduction of electron-withdrawing substituents of even moderate strength into the cyclopropane ring leads to a substantial shift of the cyclopropanediazonium ion—diazocyclopropane equilibrium to the latter compound.

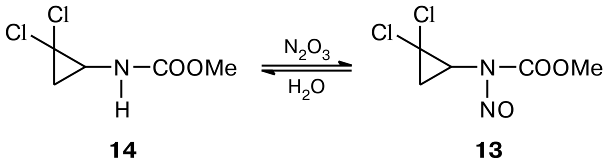
We also studied properties of methyl *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosocarbamate (**13**), which was considered as a more convenient source of 2,2-dichloro-1-diazocyclopropane compared to nitrosourea **2**. Both the NH and NH_2 groups of urea **10** are simultaneously nitrosated (Scheme 7), which complicates isolation of nitroso compound **2** from the reaction mixture[1] and, as a consequence, its yield is at most 30%.

Scheme 7



There is no problem with selectivity of nitrosation in the synthesis of nitrosourethane **13**. However, samples of compound **13** always contained noticeable amounts of the starting methyl *N*-(2,2-dichlorocyclopropyl)carbamate (**14**). The latter is formed upon storage of a solution of nitroso compound **13** in CH_2Cl_2 containing traces of water over Na_2SO_4 at 5 °C for ~16 h (Scheme 8, see also Experimental).

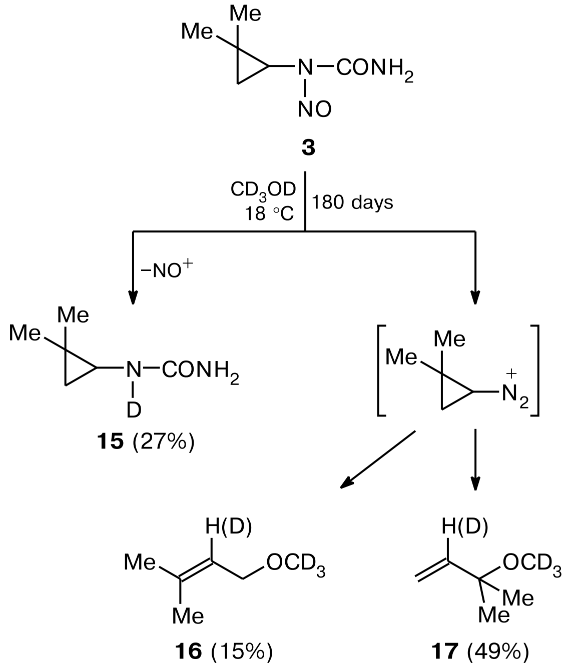
Scheme 8



Denitrosation of nitrosocarbamate **13** under the action of water occurs rather rapidly. In one experiment, the degree of denitrosation at 5 °C was ~30% after ~16 h, and the yellow solution of nitroso compound **13** in CH_2Cl_2 gradually discolored during further storage and became completely colorless after 4 days. The ^1H NMR spectrum of the resulting solution unambiguously indicated that nitrosourethane **13** was transformed into urethane **14**. The denitrosation rate of compound **13** depends apparently on the presence of traces of water and acid in CH_2Cl_2.

To the contrary, the introduction of electron-donating substituents into the cyclopropane ring of CNU substantially stabilizes this class of nitroso compounds, which was demonstrated with *N*-(2,2-dimethylcyclopropyl)-*N*-nitrosourea (**3**). Even half a year after the preparation of a solution of nitrosourea **3** in CD_3OD, the reaction mixture contained ~6% of the starting compound (its half-life is ~43 days). Decomposition of nitrosourea **3** affords urea **15** and isomeric ethers **16** and **17** (Scheme 9) as the major products, whose NMR spectra have been described earlier.[19]

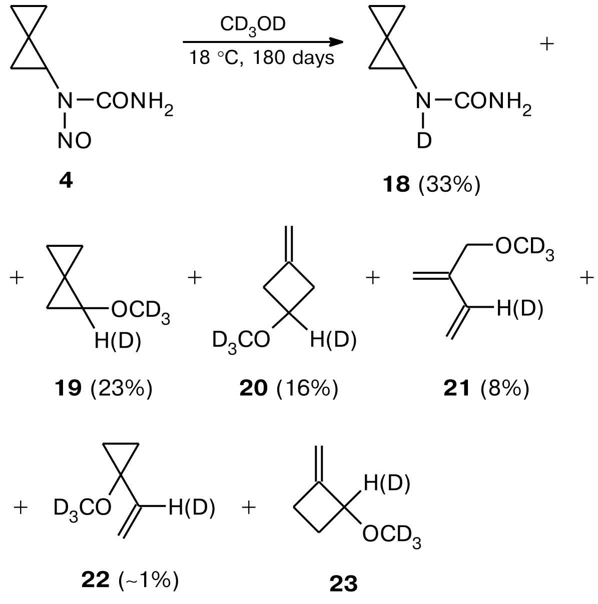
Scheme 9



The deuterium content at position 2 of allyl ethers **16** and **17** is ~57%, which is comparable with the degree of deuteration of allyl ether **8** derived from unsubstituted CNU under analogous conditions. Nitrosourea **3** does not give the corresponding cyclopropyl ether, which may be associated with the steric factors hindering the S_N2 reaction of the dimethylcyclopropanediazonium ion with methanol.

A study of a close structural analog of nitrosourea **3**, *viz.*, *N*-nitroso-*N*-spiropentylurea (**4**), showed that an increase in strain in the cyclopropane ring of CNU has no noticeable effect on the stability of this compound in methanol. The concentrations of nitroso compounds **3** and **4** decrease virtually synchronously during decomposition of these compounds. After half a year, the concentration of nitrosourea **4** in solution is 4—5%. However, it is more difficult to monitor decomposition of nitrosourea **4** by ^1H NMR spectroscopy because of a large number of compounds formed (Scheme 10).

Scheme 10



Solvolysis of nitrosourea **4** afforded *N*-spiropentylurea (**18**) and, strange as it may seem, methoxyspiropentane (**19**) as the major products; the reaction also produced 1-methoxy-3-methylidenecyclobutane (**20**) in a comparable amount. Other compounds (some of which remained unidentified) were generated in smaller amounts as a result of the cyclopropane ring opening and several successive cationoid rearrangements. The pathways of possible rearrangements of spiropentane derivatives were studied in sufficient detail. In particular, the mechanisms of formation of the products through the rearrangements of the spiropentyl cation have been considered.[20]

The ^{1}H NMR spectrum of the reaction mixture obtained upon decomposition of nitrosourea **4** is rather complicated. Fortunately, the spectra of the majority of the products have been described in the literature, and there is at least one nonoverlapping signal for each identified compound, which allows estimation of the yields of the reaction products. Urea **18** is characterized by two doublets of doublets at δ 2.81 and 1.20 corresponding to the H(1) and H_a(2) protons, respectively. Methoxyspiropentane (**19**) is characterized by a signal for the methine proton at δ 3.44. Methoxycyclobutane **20** gives a quintet of the methine proton (δ 3.93) and a triplet of triplets of the $=CH_2$ group at δ 4.83.[21] 2-(Methoxymethyl)butadiene **21** has a characteristic doublet of doublets at δ 6.38 (=CH) and a broadened singlet at δ 4.11 ($C\underline{H}_2$—OCD_3).[22] Vinylcyclopropane **22** can be identified from the doublet of doublets of the =CH group at δ 5.61.[23]

Although 1-methoxy-2-methylidenecyclobutane (**23**) would be expected[20] to be produced in small amounts (<4%), the presence of this compound in the reaction mixture cannot be stated with certainty because the ^{1}H NMR spectrum of this compound, as well as the spectra of all other 1-alkoxy-2-methylidenecyclobutanes, has not been described in the literature. Presumably, several low-intensity complex multiplets at δ 2.10—2.45 correspond to four protons of the cyclobutane ring of compound **23**.

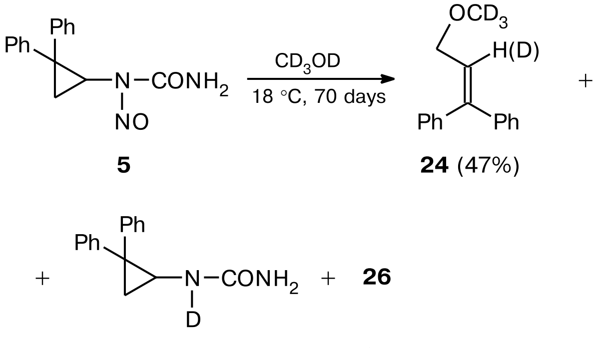
The ^{1}H NMR spectrum of methoxyspiropentane (**19**) has not been described in the literature, although the formation of compound **19** was observed[20a] upon decomposition of nitrosospiropentylurea **4** under the action of $NaHCO_3$ in MeOH. We isolated a mixture of ethers **19**—**22** from the reaction mixture and described the spectrum of compound **19** rather correctly (as far as it was possible for the partially deuterated compound).

Because of partial overlap of the signals of compounds **19**—**22** in the ^{1}H NMR spectrum, we managed to precisely determine the degrees of deuteration only for cyclobutane **20** (~48% D) and diene **21** (~53% D). The signals for the protons of the cyclopropane rings of both spiropentane **19** and vinylcyclopropane **22** appear at high field (δ 0.7—1.0). However, since the amount of the latter is rather small, a comparison of the integral intensities of the high-field multiplets and the signal for the methine proton of methoxyspiropentane **19** suggests that the degree of deuteration of compound **19** at position 1 is ~50%, *i.e.*, it is close to those observed for compounds **20** and **21**. A doublet of doublets for the proton of =CH at δ 5.61 is the only nonoverlapping signal of compound **22**. However, it is this proton that is partly replaced by deuterium. Hence, the yield of compound **22** cannot be judged from the integral intensity of this signal. Assuming that the degree of deutration of vinylcyclopropane **22** at position 1′ is equal to that of other methoxy derivatives **19**—**21** (~50%), the yield of product **22** can be estimated to be 1—1.5%.

It should be noted that the signal for the methine proton of the cyclopropane ring is always shifted downfield by ~0.1 ppm on going from nitrosourea to the corresponding urea for the entire series of cyclopropylureas. Thus the signals for the methine protons in the spectra of spiropentylureas **18** and **4** are observed at δ 2.81 and 2.71, respectively.

In its stability in CD_3OD, diphenyl-substituted nitrosourea **5** occupies an intermediate position between nitrosoureas **3** and **4**, on the one hand, and nitrosoureas **1** and **2**, on the other hand. It completely decomposes at 20 °C within 70 days, a half of nitrosourea **5** being transformed into 3,3-diphenyl-1-(trideuteriomethoxy)prop-2-ene (**24**) (Scheme 11). The ^{1}H NMR spectrum of the latter contains a doublet at δ 3.95 (2 H(1)) and a triplet at δ 6.18 (H(2)), which is consistent with the published data.[24] The doublet of the OCH_2 group is somewhat distorted due to overlap with the signal of the isotopomer containing the deuterium atom at position 2. The degree of deuteration of methoxypropene **24** at position 2 was ~15% (Table 1). Hence, it follows that the ratio of the dediazotization and deuterium exchange rates in the 2,2-diphenylcyclopropanediazonium ion is the largest of all the above-mentioned cyclopropanediazonium ions.

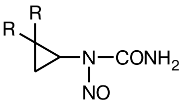
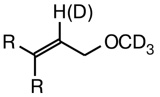
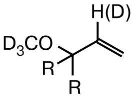
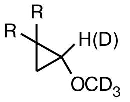
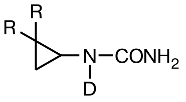
Scheme 11



The ^{1}H NMR spectrum of the denitrosation product, *viz.*, urea **25**, shows two characteristic signals, *viz.*, a doublet of doublets at δ 3.36 (H(1)) and a multiplet at δ 1.52 (2 H(3)) analogous to the signals of the authentic sample prepared earlier according to the known procedure.[25]

Unfortunately, we failed to identify minor product **26**, although we isolated this compound (~0.8 mg) from the reaction mixture in pure form. The mass spectrum of compound **26** has a molecular ion peak at *m/z* 300 (which is 19 units larger than the molecular mass of the starting nitrosourea **5**). The first ion formed upon fragmentation corresponds to the loss of the fragment with a molecular

Table 1. Decomposition of 2,2-disubstituted *N*-cyclopropyl-*N*-nitrosoureas in CD_3OD at 18 °C

Starting CNU	Yields of products (degree of deuteration) (%)				Time of complete decomposition of CNU/days
					
R = H (**1**)	84 (60)[a]	—	7 (60)[b]	4	47
R = Cl (**2**)	27 (100)	12[c] (100)	—	39	19
R = Me (**3**)	15 (58)	49 (56)	—	27	>180
R + R = $(CH_2)_2$ (**4**)	—	~25[d] (~50)	23 (~50)	33	>180
R = Ph (**5**)	47 (15)	—	—	27	70

[a] The degree of deuteration at position 2.

[b] The degree of deuteration at position 1.

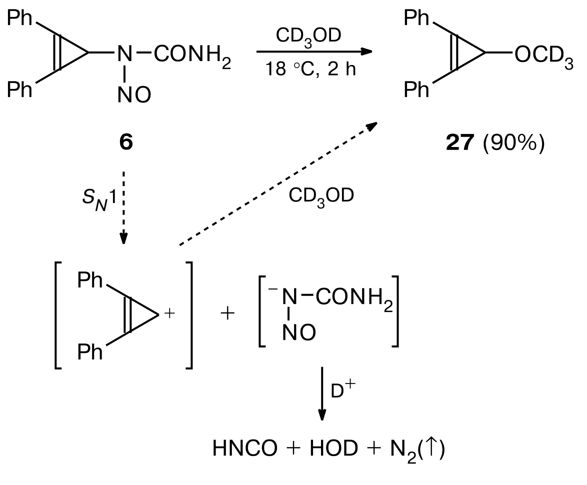
[c] The yield of $CH_2=CD-COOCD_3$.

[d] The total yield of a mixture of methoxy derivatives **20**—**22**.

mass of 35 units (CD_3OH). The ^1H, ^{13}C, DEPT-135, and HMBC NMR spectra suggest that molecule **26** contains the $-CPh_2-CH-CH_2-$ fragment. On the whole, it can be stated that compound **26** most likely has a cyclic structure with a ring size larger than three atoms. Apparently, this compound is formed with the involvement of NO^+ or HNCO present in the reaction mixture.

The character of decomposition of *N*-(2,3-diphenylcycloprop-2-enyl)-*N*-nitrosourea (**6**) in CD_3OD differs substantially from that observed for CNU containing no double bonds in the ring. Gas evolution was observed immediately after the addition of CD_3OD to nitrosourea **6**. After ~2 h (^1H NMR spectroscopic data), $\leq 10\%$ of the starting compound remained in the solution, and 2,3-diphenyl-1-(trideuteriomethoxy)cycloprop-2-ene (**27**) was present as the major product (Scheme 12). Further storage of the reaction mixture afforded several unidentified minor compounds.

Scheme 12



6

27 (90%)

Decomposition of nitrosourea **6** under the action of MeONa in MeOH gave 1-methoxy-2,3-diphenylcycloprop-2-ene (**28**)* in virtually quantitative yield. The structure of **28** was confirmed by NMR spectroscopy, mass spectrometry, and elemental analysis.

Reasoning from the high rate of transformation of compound **6** into methoxycyclopropene **27** and the absence of deuterium exchange for the methine proton of the cyclopropene ring, we believe that the reaction can proceed not through the corresponding diazonium ion, as in the case of other CNU, but through the formation of the diphenylcyclopropenyl cation due to the heterolytic C—N bond cleavage in the starting nitrosourea **6**. In terms of this scheme, the methine proton of cyclopropene **27** cannot be exchanged for deuterium. The cyclopropenediazonium ion, even though it appears, loses nitrogen too rapidly and is transformed into the thermodynamically favorable cyclopropenyl cation, thus excluding deuterium exchange, the more so as the proton abstraction from the cyclopropenediazonium ion to form 1-diazo-2,3-diphenylcycloprop-2-ene should be unfavorable due to the antiaromatic nature of the diazocyclopropene ring.[26,27]

In summary, it can be stated that all the CNU studied decompose in CD_3OD much more rapidly than MNU, decomposition involving denitrosation untypical of MNU under these conditions. The addition of acids substantially accelerates decomposition of CNU. The degree of denitrosation is the smallest for unsubstituted CNU.

The time of complete decomposition of nitrosocyclopropylureas depends substantially on the nature of substituents in the cyclopropane ring. The introduction of two Cl atoms accelerates decomposition of CNU by a

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* Attempts to trap diphenylcyclopropenylidene, 1-diazo-2,3-diphenylcycloprop-2-ene, or the corresponding diazonium ion formed upon decomposition of nitrosourea **6** with bases (Pr^iOK, MeONa, K_2CO_3) in the presence of appropriate substrates failed.

factor of 2.5, and two Me groups, to the contrary, decrease the decomposition rate by a factor of 4.5 (see Table 1). An increase in strain of the ring in nitrosospiropentylurea compared to that in dimethyl-containing CNU has no substantial effect on the decomposition rate of these nitroso compounds in methanol.

Nitrosourea **6** containing a double bond in the three-membered ring differs from other CNU under study in that it very rapidly decomposes in methanol. Apparently, the mechanism of decomposition of nitrosourea **6** may be related to the ease of formation of the aromatic cyclopropenyl cation. Presently, we have no explanation for why nitrosocyclopropylureas are more labile than their acyclic analogs in solvolysis in methanol. We have preliminary data providing evidence that CNU decompose in water even more rapidly, denitrosation playing a more substantial role. Therefore, cyclopropyl-substituted nitrosoureas can be considered as potential NO donors, which have greater capabilities to generate NO compared to the simplest *N*-alkyl-*N*-nitrosoureas. Studies in this field will undoubtedly be continued.

Experimental

The ^{1}H NMR spectra were measured on Bruker AM-300 (300 MHz) and Bruker DRX-500 (500 MHz) spectrometers for solutions containing 0.05% Me_4Si as the internal standard. The ^{13}C NMR spectra were recorded on a Bruker WM-250 (62.9 MHz) spectrometer for solutions in CD_3OD (δ_C 49.0) or $CDCl_3$ (δ_C 77.1). The mass spectra were obtained on a Finnigan MAT INCOS-50 instrument (EI, 70 eV, direct inlet). Nitrosoureas **1**,[28] **2**,[1] **3**,[29] **4**,[30] and **5** [25] were synthesized according to procedures described earlier. Diphenylcyclopropenylnitrosourea **6** was prepared analogously to the *N*′,*N*′-dimethyl-substituted analog.[26]

Preparation of solutions of nitrosoureas in CD_3OD. *N*-Cyclopropyl-*N*-nitrosoureas **1**—**6** or *N*-methyl-*N*-nitrosourea (50 μmol) was placed in an NMR tube with a tight-fitting Teflon lid, and then CD_3OD (0.4 mL) was added. All nitrosoureas completely dissolved, except for diphenylureas **5** and **6**. A half of compounds **5** and **6** dissolved and complete dissolution occurred during the reaction. The ^{1}H NMR spectra of *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosourea (**2**), *N*-(2,2-dimethylcyclopropyl)-*N*-nitrosourea (**3**), and MNU are identical to those described earlier.[29,13] Since the ^{13}C NMR spectrum of nitrosourea **2** was not reported in the study,[29] and the spectrum of nitrosourea **3** was erroneous, the spectra of these compounds are given below.

***N*-Cyclopropyl-*N*-nitrosourea (1).** ^{1}H NMR (CD_3OD), δ*: 0.57 (m, 2 H, *trans*-H(2), *trans*-H(3)); 1.02 (m, 2 H, *cis*-H(2), *cis*-H(3)); 2.36 (tt, 1 H, H(1), J_{trans} = 4.1 Hz, J_{cis} = 7.1 Hz). ^{13}C NMR (CD_3OD), δ: 7.9 (C(2), C(3)); 23.4 (C(1)); 157.4 (C=O).

***N*-(2,2-Dichlorocyclopropyl)-*N*-nitrosourea (2).** ^{13}C NMR (CD_3OD), δ: 29.1 (C(3)); 39.5 (C(1)); 58.8 (C(2)); 155.9 (C=O).

***N*-(2,2-Dimethylcyclopropyl)-*N*-nitrosourea (3).** ^{13}C NMR (CD_3OD), δ: 19.9 (C(3)); 20.5 (C(2)); 21.5, 24.5 (2 Me); 36.3 (C(1)); 157.7 (C=O).

***N*-Nitroso-*N*-spiropentylurea (4).** ^{1}H NMR (CD_3OD), δ: 0.64—0.77 (m, 2 H); 0.81—0.90 (m, 1 H); 1.07 (m, 2 H); 1.53 (br.t, 1 H, H(2), $J \approx 6.4$ Hz); 2.71 (br.dd, 1 H, H(1), $J \approx 4.0$ Hz, $J \approx 7.0$ Hz). ^{13}C NMR (CD_3OD), δ: 5.3 (CH_2); 6.6 (CH_2); 14.7 (C(2)); 17.7 (C(3)); 30.7 (C(1)); 157.4 (C=O).

***N*-(2,2-Diphenylcyclopropyl)-*N*-nitrosourea (5).** ^{1}H NMR (CD_3OD), δ: 1.74 (dd, 1 H, H(3), J_{gem} = 7.1 Hz, J_{cis} = 8.5 Hz); 2.51 (dd, 1 H, H(3), J_{trans} = 5.3 Hz, J_{gem} = 7.1 Hz); 3.29 (dd, partially overlapped with a signal of the solvent, H(1), J_{trans} = 5.3 Hz, J_{cis} = 8.5 Hz); 7.01 (m, 2 H); 7.10 (m, 3 H); 7.23 (m, 1 H); 7.33 and 7.61 (both m, 2 H each). ^{13}C NMR ($CDCl_3$), δ: 19.1 (C(3)); 37.1 (C(1)); 37.3 (C(2)); 126.8 (*p*-C arom.); 127.2 (*p*-C arom.); 127.9 (2 CH); 128.4 (2 CH); 128.7 (2 CH); 129.7 (2 CH); 138.2 (*i*-C arom.); 143.5 (*i*-C arom.); 154.6 (C=O).

***N*-(2,3-Diphenylcycloprop-2-enyl)urea** was prepared from 2,3-diphenylcycloprop-2-enecarboxylic acid[31] without purification of intermediates using a sequence of procedures that has been described earlier[26] for the synthesis of *N*-(2,3-diphenylcycloprop-2-enyl)-*N*′,*N*′-dimethyl-*N*-nitrosourea, and using ammonia instead of dimethylamine in the last step. The total yield was 86%, colorless crystals poorly soluble in most solvents, m.p. 210—214 °C (with decomp.). The ^{1}H NMR spectrum shows signals of two conformers with the integral intensity ratio of ~10 : 1. The ^{1}H NMR spectrum of the major conformer (DMSO-d_6), δ: 3.80 (d, 1 H, H(1), $^3J_{\mathrm{C\underline{H},NH}}$ = 4.4 Hz); 5.26 (br.s, 2 H, NH_2); 6.34 (br.d, 1 H, NH, $^3J_{\mathrm{CH,N\underline{H}}}$ = 4.4 Hz); 7.40—7.48 (ddt, 2 H, *p*-H arom., ^4J = 1.3 Hz, ^3J = 6.4 Hz, ^3J = 8.3 Hz); 7.50—7.58 and 7.82—7.89 (both m, 4 H each). ^{13}C NMR (DMSO-d_6), δ: 27.3 (C(1)); 117.6 (C(2), C(3)); 127.8 (2 *i*-C arom.); 128.7 (4 CH); 128.9 (2 *p*-C arom.); 129.6 (4 CH); 159.7 (C=O). The ^{1}H NMR spectrum of the minor conformer (DMSO-d_6), δ: 3.87 (d, 1 H, H(1), $^3J_{\mathrm{C\underline{H},NH}}$ = 4.3 Hz); 5.26 (br.s, 2 H, NH_2); 6.09 (br.d, 1 H, NH, $^3J_{\mathrm{CH,N\underline{H}}}$ = 4.3 Hz); 7.40—7.48 (ddt, 2 H, *p*-H arom., ^4J = 1.3 Hz, ^3J = 6.4 Hz, ^3J = 8.3 Hz); 7.50—7.58 and 7.82—7.89 (both m, 4 H each). The partial mass spectrum, *m/z* (I_{rel} (%)): 250 $[M]^+$ (14), 221 $[M - HCO]^+$ (22), 206 $[M - CONH_2]^+$ (44), 178 $[Ph—C=C—Ph]^+$ (38), 44 (100).

***N*-(2,3-Diphenylcycloprop-2-enyl)-*N*-nitrosourea (6).** Nirosation of *N*-(2,3-diphenylcycloprop-2-enyl)urea was carried out according to a procedure used for the preparation of *N*-(2,3-diphenylcycloprop-2-enyl)-*N*′,*N*′-dimethyl-*N*-nitrosourea.[26] The yield was 61%, pale-yellow crystals rapidly decompose in MeOH, m.p. 104—105 °C. Found (%): C, 68.99; H, 4.53; N, 14.89. $C_{16}H_{13}N_3O_2$. Calculated (%): C, 68.81; H, 4.69; N, 15.04. ^{1}H NMR ($CDCl_3$), δ: 3.93 (s, 1 H, H(1)); 5.17 and 6.80 (both br.s, 1 H each, NH); 7.40—7.55 (m, 6 H); 7.88 (m, 4 H). ^{13}C NMR ($CDCl_3$), δ: 31.5 (C(1)); 114.8 (C(2), C(3)); 127.6 (2 *i*-C arom.); 128.7 (4 CH); 129.6 (2 *p*-C arom.); 130.3 (4 CH); 155.2 (C=O). The partial mass spectrum, *m/z* (I_{rel} (%)): 279 $[M]^+$ (1), 249 $[M - NO]^+$ (27), 191 $[M - N(NO)CONH_2]^+$ (100), 178 $[Ph—C=C—Ph]^+$ (75).

Decomposition of *N*-methyl-*N*-nitrosourea in CD_3OD. Fourty days after the preparation of a solution of MNU in CD_3OD, the ^{1}H NMR spectrum contained a singlet at δ 3.12 belonging to the starting compound and a singlet at δ 2.68 corresponding to that

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* Hereinafter, the signals for the protons of the NH and NH_2 groups were not observed in the ^{1}H NMR spectra recorded in CD_3OD due to fast deuterium exchange with the solvent.

of the authentic sample of *N*-methylurea. The yield of *N*-methylurea was ~1%.

Decomposition of *N*-cyclopropyl-*N*-nitrosourea (1) in CD_3OD. Fourty-seven days after the preparation of a solution of nitrosourea **1** in CD_3OD, the signals corresponding to the starting compound disappeared. The resulting mixture contained (^1H NMR spectroscopic data) compounds presented in Scheme 1 and listed in Table 1.

N-Cyclopropylurea (7). ^1H NMR (CD_3OD, 500 MHz), δ: 0.47 (m, 2 H, *trans*-H(2), *trans*-H(3)); 0.69 (m, 2 H, *cis*-H(2), *cis*-H(3)); 2.45 (tt, 1 H, H(1), $J_{trans} = 3.5$ Hz, $J_{cis} = 7.0$ Hz). The ^1H NMR spectrum corresponds to the spectrum of the authentic sample prepared according to a known procedure.[28]

1-(Trideuteriomethoxy)prop-2-ene (8). ^1H NMR (CD_3OD, 500 MHz), δ: 3.917 (dt, 2 H, H(1), $^4J_{trans} \approx {}^4J_{cis} \approx 1.4$ Hz, $^3J = 5.6$ Hz); 5.165 (ddt, 1 H, H(3), $^4J_{trans} = 1.3$ Hz, $^2J = 1.9$ Hz, $^3J_{cis} = 10.4$ Hz); 5.260 (dq, 1 H, H(3), $^4J_{cis} \approx {}^2J \approx 1.7$ Hz, $^3J_{trans} = 17.3$ Hz); 5.891 (ddt, 1 H, H(2), $^3J = 5.6$ Hz, $^3J_{cis} = 10.4$ Hz, $^3J_{trans} = 17.3$ Hz).

2-Deuterio-1-(trideuteriomethoxy)prop-2-ene (**8**-d). ^1H NMR (CD_3OD, 500 MHz), δ: 3.914 (m, 2 H, H(1)); 5.163 (br.q, 1 H, H(3), $^4J_{trans} \approx {}^2J \approx {}^3J_{H,D} \approx 1.5$ Hz); 5.252 (tq, 1 H, H(3), $^4J_{cis} \approx {}^2J \approx 1.7$ Hz, $^3J_{H,D} = 2.7$ Hz).

(Trideuteriomethoxy)cyclopropanes 9 and 9-d. ^1H NMR (CD_3OD, 500 MHz), δ: 0.43—0.51 (m, 4 H, 2 H(2), 2 H(3)); 3.24 (tt, 0.4 H, residual proton at the C(1) atom, $J_{trans} = 3.0$ Hz, $J_{cis} = 6.0$ Hz).

Decomposition of *N*-cyclopropyl-*N*-nitrosourea (1) in CD_3OD in the presence of H_2SO_4. Nitrosourea **1** (6.5 mg, 50 μmol) was placed in an NMR tube, then CD_3OD (0.4 mL) was added followed by the addition of one microdrop of 95% H_2SO_4 (0.4 mg, ~4 μmol). The solution was rapidly stirred. After 70 min, 12% of the starting nitrosourea **1** decomposed (^1H NMR spectroscopic data). After 24 h, the conversion was 52%. The signals corresponding to the nitrosourea disappeared completely after 14 days. The ratio of decomposition products of CNU vary only slightly during the reaction. The final solution in CD_3OD contained *N*-cyclopropylurea (**7**) (61%), 1-(trideuteriomethoxy)prop-2-ene (**8**) (32%), trideuteriomethoxycyclopropane (**9**) (3%), and allyl alcohol (~1%), which gives a characteristic signal of the $C\underline{H}_2OH$ group as a doublet of triplets at δ 4.05 ($^4J_{trans} \approx {}^4J_{cis} \approx 1.6$ Hz, $^3J = 5.0$ Hz). Then K_2CO_3 (~2 mg) was added to the reaction mixture to neutralize H_2SO_4, and all volatile components were recondensed *in vacuo* (~0.1 Torr) to another NMR tube.

1-(Trideuteriomethoxy)prop-2-ene (**8**). ^{13}C NMR (CD_3OD), δ[*]: 74.4 (C(1)); 117.4 (C(3)); 135.9 (C(2)).

(Trideuteriomethoxy)cyclopropane (**9**). ^{13}C NMR (CD_3OD), δ: 5.7 (C(2), C(3)); 55.3 (C(1)).

Allyl alcohol. ^1H NMR (CD_3OD), δ: 4.05 (dt, 2 H, H(1), $^4J_{trans} \approx {}^4J_{cis} \approx 1.7$ Hz, $^3J = 5.1$ Hz); 5.08 (dq, 1 H, H(3), $^4J_{trans} \approx {}^2J \approx 1.8$ Hz, $^3J_{cis} = 10.4$ Hz); 5.24 (dq, 1 H, H(3), $^4J_{cis} \approx {}^2J \approx 1.8$ Hz, $^3J_{trans} = 17.2$ Hz); 5.95 (ddt, 1 H, H(2), $^3J = 5.1$ Hz, $^3J_{cis} = 10.4$ Hz, $^3J_{trans} = 17.2$ Hz). ^{13}C NMR (CD_3OD), δ: 63.9 (C(1)); 114.8 (C(3)); 138.8 (C(2)).

Methanol-d_4 (0.4 mL) was added to the first NMR tube containing a nonvolatile residue. The resulting solution contained (^1H NMR spectroscopic data) pure *N*-cyclopropylurea (**7**). The ^1H NMR spectrum corresponds to that described above. ^{13}C NMR (CD_3OD), δ: 7.3 (C(2), C(3)); 23.4 (C(1)); 163.5 (C=O).

Decomposition of *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosourea (2) in CD_3OD. Nineteen days after the preparation of a solution of nitrosourea **2** in CD_3OD, the signals corresponding to the starting compound disappeared. The mixture contained (^1H NMR spectroscopic data) *N*-(2,2-dichlorocyclopropyl)urea (**10**) (39%), trideuteriomethyl 2-deuterioacrylate (**11**) (12%), and 1,1-dichloro-2-deuterio-3-(trideuteriomethoxy)prop-1-ene (**12**) (27%). The ^1H NMR spectrum of urea **10** corresponds to that described earlier.[29]

N-(2,2-Dichlorocyclopropyl)urea (**10**). ^{13}C NMR (CD_3OD), δ: 27.4 (C(3)); 39.4 (C(1)); 60.9 (C(2)); 162.1 (C=O).

Compound **11**. ^1H NMR (CD_3OD), δ: 5.87 (q, 1 H, H(3), $^2J = {}^3J_{H,D} = 1.5$ Hz); 6.36 (dt, 1 H, H(3), $^2J = 1.5$ Hz, $^3J_{H,D} = 2.6$ Hz).

Compound **12**. ^1H NMR (CD_3OD), δ: 4.05 (t, 2 H, H(3), $^3J_{H,D} = 1.0$ Hz).

Methyl *N*-(2,2-dichlorocyclopropyl)carbamate (14). Methanol (2 mL) was added with stirring to 2,2-dichlorocyclopropyl isocyanate[29] (195 mg, 1.28 mmol) for 20 min. The reaction solution was heated to boiling and kept at this temperature for 30 min. Then the reaction mixture was concentrated, and the crystalline precipitate was recrystallized from a pentane—diethyl ether mixture (4 : 1). Urethane **14** was obtained as colorless crystals in a yield of 175 mg (74%), m.p. 69—70 °C. ^1H NMR ($CDCl_3$), δ: 1.46 (br.dd, 1 H, H(3), $J_{trans} \approx 6.7$ Hz, $J_{gem} \approx 8.5$ Hz); 1.88 (dd, 1 H, H(3), $J_{gem} = 8.5$ Hz, $J_{cis} = 9.2$ Hz); 3.34 (br.s, 1 H, H(1)); 3.74 (br.s, 3 H, OMe); 5.05 (br.s, 1 H, NH). The ^{13}C NMR spectrum is identical to that described earlier.[1]

Methyl *N*-(2,2-dichlorocyclopropyl)-*N*-nitrosocarbamate (13). A freshly prepared solution of N_2O_4 (550 mg, 6 mmol) in Et_2O (5 mL) was added with vigorous stirring to a suspension of urethane **14** (167 mg, 0.91 mmol), AcONa (500 mg, 6 mmol), and Na_2SO_4 (350 mg, 2.5 mmol) in dry CH_2Cl_2 (20 mL) under argon at –20 °C for 15 min. The intense-yellow suspension was stirred at –15—–20 °C for 40 min. Then excess N_2O_4 was distilled off *in vacuo* at the same temperature, the solution was concentrated to ~4/5 of the initial volume, and the reaction mixture was washed with brine (10 mL), a mixture of concentrated solutions of NaCl and $NaHCO_3$ (1 : 1, 2×10 mL), and brine (10 mL). All steps were carried out rapidly at a temperature no higher than 5 °C. The resulting bright-yellow solution of nitrosourethane **13** in CH_2Cl_2 was dried with anhydrous Na_2SO_4 at 5 °C for ~16 h. Then an aliquot of the solution was concentrated directly in an NMR tube, the residue was dissolved in $CDCl_3$, and NMR spectra were recorded, which demonstrated that the product contained nitrosourethane **13** and the starting urethane **14** (~7 : 3). Compound **13**. ^1H NMR ($CDCl_3$), δ: 1.98 (dd, 1 H, H(3), $J_{trans} = 6.8$ Hz, $J_{gem} = 9.3$ Hz); 2.22 (t, 1 H, H(3), $J_{cis} \approx J_{gem} \approx 9.3$ Hz); 3.05 (dd, 1 H, H(1), $J_{trans} = 6.8$ Hz, $J_{cis} = 9.5$ Hz); 4.12 (s, 3 H, OMe). ^{13}C NMR ($CDCl_3$), δ: 28.4 (C(3)); 38.8 (C(1)); 55.0 (OMe); 57.3 (C(2)); 153.6 (C=O). Further storage of a solution of nitrosourethane **13** over Na_2SO_4 at 5 °C resulted in the gradual disappearance of the yellow color characteristic of the nitroso compound. After 4 days, the solution contained (^1H NMR spectroscopic data) virtually pure urethane **14**.

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[*] Hereinafter, the signal for the C atom of the OCD_3 group was not observed in the ^{13}C NMR spectra due to its low intensity and low concentrations of the solutions under study.

Decomposition of *N*-(2,2-dimethylcyclopropyl)-*N*-nitrosourea (3) in CD_3OD. One hundred-and-eighty days after the preparation of a solution of nitrosourea **3** in CD_3OD, the mixture contained (^1H NMR spectroscopic data) the compounds presented in Scheme 9 and listed in Table 1. Volatile components were recondensed *in vacuo* (~0.1 Torr) to another NMR tube. Only methoxypropenes **16**, **16**-d, **17**, and **17**-d were identified in the condensate by ^1H NMR spectroscopy.

3,3-Dimethyl-1-(trideuteriomethoxy)prop-2-enes **16** and **16**-d. ^1H NMR (CD_3OD), δ: 1.68 and 1.75 (both br.s, 3 H each, Me); 3.91 (m, 2 H, H(1)); 5.31 (t.sept, 0.42 H, residual proton at the C(2) atom, ^4J = 1.4 Hz, ^3J = 7.0 Hz).

1,1-Dimethyl-1-(trideuteriomethoxy)prop-2-ene (**17**). ^1H NMR (CD_3OD), δ: 1.25 (s, 6 H, 2 Me); 5.15 (dd, 1 H, H(3), ^2J = 1.3 Hz, $^3J_{cis}$ = 10.8 Hz); 5.17 (dd, 1 H, H(3), ^2J = 1.3 Hz, $^3J_{trans}$ = 17.7 Hz); 5.80 (dd, 1 H, H(2), $^3J_{cis}$ = 10.8 Hz, $^3J_{trans}$ = 17.7 Hz).

2-Deuterio-1,1-dimethyl-1-(trideuteriomethoxy)prop-2-ene (**17**-d). ^1H NMR (CD_3OD), δ: 1.25 (s, 6 H, 2 Me); 5.14—5.17 (m, 2 H, H(3)).

D_2O (0.4 mL) was added to the first NMR tube containing a nonvolatile residue. The resulting solution contained (^1H NMR spectroscopic data) *N*-(2,2-dimethylcyclopropyl)urea (**15**) with an impurity of nitrosourea **3**. The solution was kept at 90 °C for 1 h and then lyophilized. Pure urea **15** was obtained as a colorless finely crystalline powder in a yield of ~1.5 mg, m.p. 140—142 °C. Found (%): C, 56.02; H, 9.07; N, 21.56. $C_6H_{12}N_2O$. Calculated (%): C, 56.23; H, 9.44; N, 21.86. ^1H NMR (CD_3OD), δ: 0.29 (br.t, 1 H, H(3), $J \approx 4$ Hz); 0.66 (dd, 1 H, H(3), J_{gem} = 5.1 Hz, J_{cis} = 7.6 Hz); 1.07 and 1.08 (both s, 3 H each, Me); 2.26 (dd, 1 H, H(1), J_{trans} = 4.0 Hz, J_{cis} = 7.6 Hz). ^{13}C NMR (CD_3OD), δ: 18.8 (C(2)); 19.4 (Me); 20.9 (C(3)); 25.1 (Me); 35.5 (C(1)); 163.6 (C=O).

Decomposition of *N*-nitroso-*N*-spiropentylurea (4) in CD_3OD. One hundred-and-eighty days after the preparation of a solution of nitrosourea **4** in CD_3OD, the mixture contained (^1H NMR spectroscopic data) compounds presented in Scheme 10 and listed in Table 1. Volatile components were recondensed *in vacuo* (~0.1 Torr) to another NMR tube. Partially deuterated ethers **19**—**22** were identified in the condensate by ^1H NMR spectroscopy.

(Trideuteriomethoxy)spiropentanes **19** and **19**-d. ^1H NMR (CD_3OD), δ: 0.75 (m, 1 H); 0.85 (m, 3 H); 0.94 (m, 2 H); 3.44 (ddd, ~0.5 H, residual proton at the C(1) atom, J = 1.3 Hz, J = 2.5 Hz, J = 5.7 Hz).

1-Trideuteriomethoxy-3-methylidenecyclobutanes **20** and **20**-d. ^1H NMR (CD_3OD), δ: 2.60 and 2.85 (both m, 2 H each, H(2), H(4)); 3.93 (quint, 0.52 H, residual proton at the C(1) atom, ^3J = 6.5 Hz); 4.83 (tt, 2 H, =CH_2, ^4J = 2.0 Hz, ^4J = 2.9 Hz).

2-(Trideuteriomethoxymethyl)buta-1,3-dienes **21** and **21**-d. Partial ^1H NMR spectrum (CD_3OD), δ: 4.11 (dd, 2 H, CH_2OCD_3, ^4J = 0.7 Hz, ^4J = 1.3 Hz); 6.38 (dd, 0.47 H, residual proton at the C(3) atom, ^3J = 11.1 Hz, ^3J = 17.9 Hz).

1-(Trideuteriomethoxy)-1-vinylcyclopropanes **22** and **22**-d. The partial ^1H NMR spectrum (CD_3OD), δ: 5.61 (dd, residual proton at the C(1´) atom, ^3J = 10.8 Hz, ^3J = 17.3 Hz).

D_2O (0.4 mL) was added to the first NMR tube containing a nonvolatile residue. The resulting solution contained (^1H NMR spectroscopic data) *N*-spiropentylurea (**18**) and an impurity of nitrosourea **4**. The solution was kept at 90 °C for 1 h and then lyophilized. Urea **18** was obtained in a yield of ~2 mg (~95% purity). The ^1H and ^{13}C NMR spectra of urea **18** are identical to those of the authentic sample prepared according to a known procedure.[30] ^1H NMR (CD_3OD), δ: 0.74—1.01 (m, 5 H); 1.20 (dd, 1 H, H(2), J_{gem} = 4.9 Hz, J_{cis} = 6.6 Hz); 2.81 (dd, 1 H, H(1), J_{trans} = 3.2 Hz, J_{cis} = 6.6 Hz). ^{13}C NMR (CD_3OD), δ: 4.1 (CH_2); 7.3 (CH_2); 15.2 (C(2)); 16.5 (C(3)); 29.7 (C(1)); 163.2 (C=O).

Decomposition of *N*-(2,2-diphenylcyclopropyl)-*N*-nitrosourea (5) in CD_3OD. Seventy days after the addition of CD_3OD to nitrosourea **5**, the signals corresponding to the starting compound disappeared. The ^1H NMR spectrum of the mixture contained a broad multiplet at δ 7.1—7.8 and signals corresponding to three compounds presented in Scheme 11 and listed in Table 1.

1-(Trideuteriomethoxy)-3,3-diphenylprop-2-enes **24** and **24**-d. Partial ^1H NMR spectrum (CD_3OD), δ: 3.95 (br.d, 2 H, H(1), ^3J = 6.8 Hz); 6.18 (t, 0.85 H, the residual proton at the C(2) atom, ^3J = 6.8 Hz).

N-(2,2-Diphenylcyclopropyl)urea (**25**). Partial ^1H NMR spectrum (CD_3OD), δ: 1.52 (m, 2 H, H(3)); 3.36 (dd, 1 H, H(1), J_{trans} = 5.7 Hz, J_{cis} = 7.4 Hz).

Compound **26**. Partial ^1H NMR spectrum (CD_3OD), δ: 2.89 (dd, 1 H, J = 8.8 Hz, J = 10.2 Hz); 3.60 (dd, 1 H, J = 1.9 Hz, J = 10.2 Hz); 4.76 (dd, 1 H, J = 1.9 Hz, J = 8.8 Hz).

The resulting solution of compounds **24**—**26** in CD_3OD was concentrated, and the residue was separated by preparative TLC (SiO_2; C_6H_6—AcOEt, 10 : 1, as the eluent). Methoxypropene **24** (R_f 0.79—0.90), urea **25** (R_f 0—0.1), and compound **26** (R_f 0.40—0.49) were isolated in yields of 4.7, 2.8, and ~0.8 mg, respectively.

Trideuteriomethoxypropenes **24** and **24**-d. ^1H NMR ($CDCl_3$), δ: 3.96 (br.d, 2 H, H(1), ^3J = 6.9 Hz); 6.18 (t, 0.85 H, the residual proton at the C(2) atom, ^3J = 6.9 Hz); 7.14 (m, 2 H); 7.24 and 7.38 (both m, 4 H each). ^{13}C NMR (CD_3OD), δ: 71.1 (C(1)); 125.9 (C(2)); 128.5 (2 CH); 128.7 (2 CH); 129.2 (2 CH); 129.3 (2 CH); 130.7 (2 *p*-C arom.); 140.5 (*i*-C arom.); 143.1 (*i*-C arom.); 146.7 (C(3)).

Urea **25**. ^1H NMR (CD_3OD), δ: 1.52 (m, 2 H, H(3)); 3.36 (dd, 1 H, H(1), J_{trans} = 5.7 Hz, J_{cis} = 7.4 Hz); 7.08—7.43 (m, 10 H). ^{13}C NMR (CD_3OD), δ: 20.5 (C(3)); 36.9 (C(1)); 37.9 (C(2)); 127.1 (*p*-C arom.); 127.6 (*p*-C arom.); 129.1 (2 CH); 129.3 (2 CH); 129.4 (2 CH); 131.5 (2 CH); 141.7 (*i*-C arom.); 146.6 (*i*-C arom.); 162.7 (C=O).

Compound **26**. The ^{14}N NMR spectrum has not intense signals. ^1H NMR ($CDCl_3$, 500 MHz), δ: 2.53 (d, 1 H, J = 2.9 Hz); 3.01 (t, 1 H, $J \approx 9.4$ Hz); 3.55 (dd, 1 H, J = 2.2 Hz, J = 9.8 Hz); 4.79 (dt, 1 H, $J \approx 2.6$ Hz, J = 9.0 Hz); 7.27—7.36 (m, 6 H); 7.41 and 7.44 (both m, 2 H each). ^{13}C NMR ($CDCl_3$), δ: 45.1 ($\underline{C}Ph_2$); 73.2 (CH); 73.6 (CH_2); 127.4 (*p*-C arom.); 127.5 (*p*-C arom.); 127.7 (2 CH); 128.0 (2 CH); 128.6 (2 CH); 128.8 (2 CH); 140.7 (*i*-C arom.); 141.5 (*i*-C arom.); 205.5 (C=O). MS (Finnigan LCQ (ESI)), *m/z*: 301 $[M + H]^+$, 266 $[M - CD_3OH]^+$.

Decomposition of *N*-(2,3-diphenylcycloprop-2-enyl)urea (6) in CD_3OD. The addition of CD_3OD to nitrosourea **6** led to weak gas evolution. After 2 h, the ^1H NMR spectrum of the solution showed signals for the protons of the benzene rings and two singlets at δ 4.41 and 3.89 with the integral intensity ratio of 14 : 1 corresponding to 2,3-diphenyl-1-(trideuteriomethoxy)cycloprop-2-ene (**27**) and nitrosourea **6**, respectively. The ^1H and ^{13}C NMR spectra of compound **27** are identical to those of the authentic sample. Further storage of the reaction mixture led to precipitation, and signals of two unidentified compounds of the cyclopropene series appeared in the ^1H NMR spectrum.

1-Methoxy-2,3-diphenylcycloprop-2-ene (28). A suspension of MeONa (76 mg, 1.4 mmol) in a 3 : 1 CH_2Cl_2—MeOH mixture (5 mL) was cooled to −20 °C, and then nitrosourea **6** (110 mg, 0.39 mmol) was added portionwise with stirring for 45 min, whereupon vigorous gas evolution occurred. The reaction mixture was allowed to warm to ~20 °C, the residue was filtered off, and the filtrate was concentrated. Methoxypropene **28** was obtained as a yellowish oil in a yield of 82 mg (94%). Found (%): C, 86.69; H, 6.53. $C_{16}H_{14}O$. Calculated (%): C, 86.45; H, 6.35. ^1H NMR (CD_3OD), δ: 3.44 (s, 3 H, OMe); 4.39 (s, 1 H, H(1)); 7.42 (m, 2 H); 7.51 and 7.77 (both m, 4 H each). ^{13}C NMR (CD_3OD), δ: 56.51 (OMe); 56.91 (C(1)); 122.24 (C(2), C(3)); 129.39 (2 *i*-C arom.); 130.06 (4 CH); 130.55 (2 *p*-C arom.); 130.93 (4 CH). The partial mass spectrum, m/z (I_{rel} (%)): 221 $[M]^+$ (30), 191 $[M - OMe]^+$ (100), 178 $[Ph—C=C—Ph]^+$ (99).

We found that storage of a solution of compound **28** in $CHCl_3$ containing traces of EtOH resulted in partial conversion of 1-methoxy-2,3-diphenylcycloprop-2-ene (**28**) into 1-ethoxy-2,3-diphenylcycloprop-2-ene. ^1H NMR (CD_3OD), δ: 1.20 (t, 3 H, $OCH_2\underline{CH}_3$, ^3J = 7.0 Hz); 3.73 (q, 2 H, OCH_2, ^3J = 7.0 Hz); 4.41 (s, 1 H, H(1)); 7.42 (m, 2 H); 7.51 and 7.77 (both m, 4 H each). ^{13}C NMR (CD_3OD), δ: 15.89 ($OCH_2\underline{C}H_3$); 55.51 (C(1)); 65.58 (OCH_2); 122.25 (C(2), C(3)); 129.43 (2 *i*-C arom.); 130.03 (4 CH); 130.49 (2 *p*-C arom.); 130.90 (4 CH).

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