Generation and reactions of diazo-3,3-dideuterio-2-methylidenecyclopropane and isomerization of 3´,3´-dideuterio-2´-methylidenespiro[4,5-dihydropyrazole-5,1´-cyclopropanes] into isopropenylpyrazoles*

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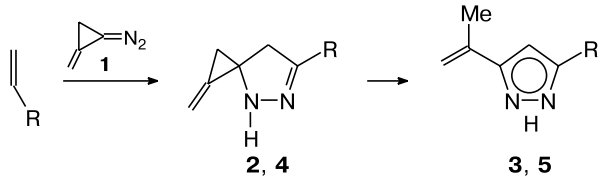
N-(1,3,3-Trideuterio-2-methylidenecyclopropyl)-*N*-nitrosourea was synthesized and its decomposition on treatment with K_2CO_3 in the presence of acrylonitrile and ethyl acrylate or on treatment with MeONa in the absence of unsaturated substrates was studied. The rate of decomposition of the nitrosourea is much lower than that of the nondeuterated analog. The use of acrylates for trapping the intermediate 3,3-dideuterio-1-diazo-2-methylidenecyclopropane results in the corresponding 2´-methylidenespiro[4,5-dihydropyrazole-5,1´-cyclopropanes] containing two deuterium atoms in the cyclopropane fragment. The resulting dihydropyrazoles are isomerized almost entirely over a period of 1—3 days to give a mixture (~1 : 1) of isopropenylpyrazoles in which both deuterium atoms occur either in the methyl or in the methylidene groups of the isopropenyl substituent. A possible mechanism of this transformation is considered.

Key words: deuterium-containing methylidenecyclopropanes, 2´-methylidenespiro[4,5-dihydropyrazole-5,1´-cyclopropanes], isopropenylpyrazoles, 1,3-dipolar cycloaddition, isomerization, ^{1}H and ^{13}C NMR spectroscopy.

Previously,[1] we showed that the reaction of diazo-2-methylidenecyclopropane (**1**) generated *in situ* with acrylonitrile occurs as 1,3-dipolar cycloaddition and that 2´-methylidene-3-cyanospiro[4,5-dihydropyrazole-5,1´-cyclopropane] (**2**) thus formed, unlike 3-cyanospiro[4,5-dihydropyrazole-5,1´-cyclopropane] containing no exocyclic double bond,[2] partially isomerizes during the reaction (0 °C, 3 h) into 5(3)-isopropenyl-3(5)-cyanopyrazole (**3**). The complete transformation **2** → **3** required 36 h, pyrazole **3** being isolated from the reaction mixture in ~65% yield (Scheme 1).

Scheme 1



2, **4** **3**, **5**

R = CN (**2**, **3**); COOEt (**4**, **5**)

This type of transformation also takes place for other analogous dihydropyrazoles. In particular, we showed using ^{1}H NMR spectroscopy that 2´-methylidene-3-ethoxycarbonylspiro[4,5-dihydropyrazole-5,1´-cyclopropane] (**4**), formed in the reaction of ethyl acrylate with diazo(methylidene)cyclopropane **1** generated from *N*-(2-methylidenecyclopropyl)-*N*-nitrosourea on treatment with K_2CO_3 at 0 °C, underwent selective isomerization over a period of 2.5 h into 5(3)-isopropenyl-3(5)-ethoxycarbonylpyrazole (**5**), which was isolated in 62% yield. Previously,[3] compound **5** was prepared by long-term storage (6 months) of a solution of ethyl diazoacetate and isopropenylacetylene in ether; however, it was not characterized by spectroscopy.

In the present work, we studied the mechanism of rearrangement of methylidenespiro[4,5-dihydropyrazole-cyclopropanes] into isopropenylpyrazoles. Dihydropyrazoles **2**-d_2 and **4**-d_2 deuterium-labeled in the cyclopropane ring used in the study were prepared as shown in Scheme 2.

This transformation can, in principle, follow several alternative pathways. According to one of them, this is a pericyclic reaction including a sigmatropic shift of the H atom from the dihydropyrazole ring to the methylene or

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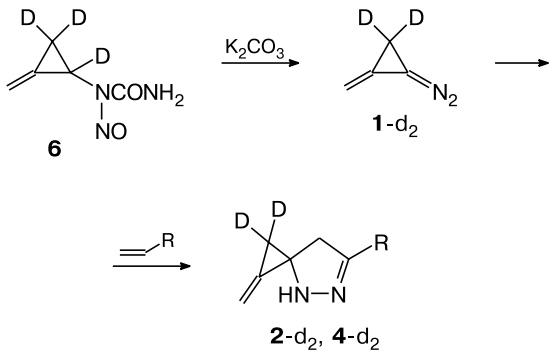
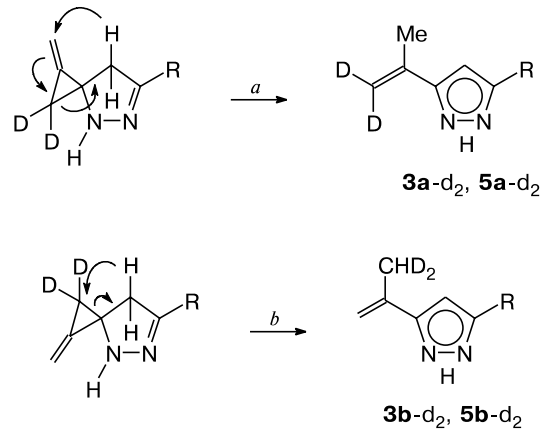
Scheme 2



R = CN (**2**), COOEt (**4**)

methylidene group of the methylidenecyclopropane fragment. The deuterium label should be either fully retained at the double bond of the isopropenyl group (Scheme 3, pathway *a*) or be incorporated in the methyl group (pathway *b*).

Scheme 3



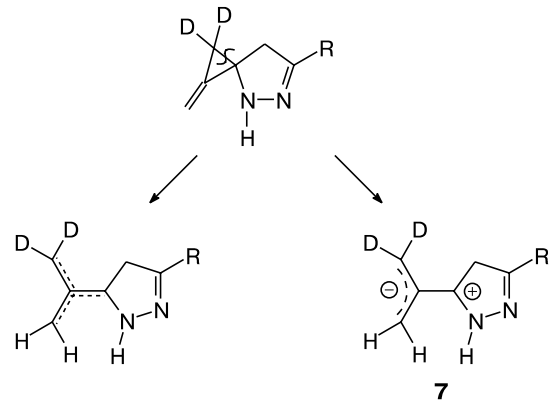
R = CN (**3**), COOEt (**5**)

In addition, the reaction can proceed as a trimethylenemethane rearrangement with the intermediate formation of a biradical or zwitter-ion **7** upon cleavage of the σ-bond opposing the exomethylene fragment in the cyclopropane ring (Scheme 4). In this case, due to equivalence of the CH_2 and CD_2 groups, the subsequent formation of the isopropenyl group should result in deuterium labeling of either the methylidene or the methyl group, *i.e.*, a mixture of **3a**-d_2 and **3b**-d_2 or **5a**-d_2 and **5b**-d_2 should be formed.

Results and Discussion

In order to prepare deuterated spiro[dihydropyrazolecyclopropanes] **2**-d_2 and **4**-d_2, we first synthesized

Scheme 4



N-(2-methylidenecyclopropyl)-*N*-nitrosourea (**6**) containing three deuterium atoms in the cyclopropane ring starting from 1,3,3-trideuterio-2-methylidenecyclopropanecarboxylic acid (**8**) and using procedures we employed previously[1] to prepare the nondeuterated analog.

A convenient method for the synthesis of methylidenecyclopropanecarboxylic acid includes metallation of methylidenecyclopropane on treatment with BuLi with subsequent carbonization. A previous study[4] describes the synthesis of 2,2,3,3-tetradeuteriomethylidenecyclopropane by deuterium exchange of the cyclopropane ring protons in methylidenecyclopropane on treatment with $D_3CSOCD_2^-Na^+$ in DMSO-d_6 (reactant molar ratio 1 : 0.5 : 4.7, 36 h at 25 °C, yield 80%, deuterium content 76—77%). We found that the use of $D_3CSOCD_2^-K^+$ reduces substantially the time of deuterium exchange. According to experiments carried out directly in the NMR tube, at a methylidenecyclopropane : $D_3CSOCD_2^-K^+$: DMSO-d_6 molar ratio equal to 1 : 0.3 : 9, the degree of deuteration* of methylidenecyclopropane is ~75% of the theoretical value 20 min after mixing the reactants, and after 2 h, the deuterium exchange can be considered complete (~93%). Further increase in the deuterium exchange time results in a gradual decrease in the yield of methylidenecyclopropane. Taking into account these observations, we developed a procedure that allowed the preparation of multigram quantities of deuterated methylidenecyclopropane with any degree of deuteration.

However, the next step, *i.e.*, the preparation of acid **8**, was faced with substantial difficulties. It was found that methylidenecyclopropane-d_4 (~95% D) reacts with BuLi much more slowly than the nondeuterated analog. Indeed, although the time of exposure of the reaction mix-

* The degree of deuteration of methylidenecyclopropane (and other labeled compounds) was determined on the basis of ^{1}H NMR spectra by comparing the integral intensities of the residual proton signals of the cyclopropane ring and the olefinic protons containing no deuterium labels.

ture at 0 °C was increased from 20 min[5] to 1 h, treatment of the mixture with CO_2 gave a mixture of valeric and methylidenecyclopropanecarboxylic-d_3 acid in ~5 : 1 molar ratio, the overall yield being only 30—35%, which suggested that metallation did not proceed to completion. The low degree of conversion of methylidenecyclopropane-d_4 into acid **8** is due to a substantial isotope effect involved in this reaction, which is no less than 10, according to our estimates. It is generally accepted that the primary k_H/k_D isotope effect for reactions where hydrogen atom transfer is the rate-determining step equals 5 or more.[6] In our case, in addition to the primary isotope effect, secondary isotope effects caused by the three adjacent deuterium atoms are to be taken into account.

Due to the difficulty of separation of the acids and the low yield of the target product, we employed a stronger metallating agent, *viz.*, potassium tetramethylpiperidide, prepared at −95 °C by adding a solution of BuLi in hexane to a suspension of Bu^{t}OK and 2,2,6,6-tetramethylpiperidine in THF. The reaction of this reagent with methylidenecyclopropane-d_4 was carried out at −80 to −60 °C for 25 min; then the reaction mixture was poured onto solid CO_2. In this case, usual workup gave only acid **8**; however, its yield was rather low (11—13%). Besides, the degree of deuteration of the resulting acid somewhat decreased (by 6—8%) compared to the initial sample of deuterated methylidenecyclopropane.

Acid **8** was further converted into nitrosourea **6** without any problems using previously described procedures.[1] According to ^{1}H NMR spectrum, the ratio of the integral intensities of the CH= proton signal and the signal of any of the residual protons of the cyclopropane ring is ~7 : 1. It is worth noting that pronounced decomposition of nitrosourea **6** on treatment with MeONa in CD_3OD, which can be monitored by low-temperature ^{1}H NMR spectroscopy, starts at −20 °C, whereas decomposition of nondeuterated analog begins at −50 °C, which is apparently also due to the kinetic isotope effect. The substantial magnitude of this effect may imply that proton abstraction from the carbon atom linked to nitrogen is the rate-determining step in the alkaline hydrolysis of *N*-nitrosoureas. As expected,[1] butatriene-1,1-d_2 was formed as the major reaction product, whose yield calculated from the integral intensities of the butatriene signal with δ 5.34 and the signal of *p*-dibromobenzene added in a known amount as the reference was ~80%.

The lower rate of decomposition of deuterated nitrosourea **6** compared to the nondeuterated analog is clearly manifested also in the reaction with K_2CO_3 in the presence of acrylonitrile or ethyl acrylate. Indeed, in the trapping of diazomethylidenecyclopropane (**1**-d_2), generated *in situ*, with acrylonitrile at 0 °C, complete conversion of nitrosourea **6** is observed only after 24—25 h, whereas the nondeuterated specimen is converted over a period of ~2 h (see Ref. 1). According to the ^{1}H NMR spectrum, the reaction yields a mixture of spiro[dihydropyrazole-5,1′-cyclopropane] **2**-d_2 and pyrazoles (**3a**+**3b**)-d_2 in ~3.3 : 1 ratio. As expected, spiro compound **2**-d_2 has both deuterium atoms in the cyclopropane fragment, the **3a**-d_2 to **3b**-d_2 isomer ratio being ~1.2 : 1. The last-mentioned fact indicates that isomerization of spiro[dihydropyrazole-5,1′-cyclopropanes] into isopropenylpyrazoles is not a concerted process. Storage of the obtained reaction mixture for additional 2 days at 20 °C results in almost complete conversion of **2**-d_2. Pyrazole **3**-d_2 was isolated by TLC as a crystalline solid in 52% yield.

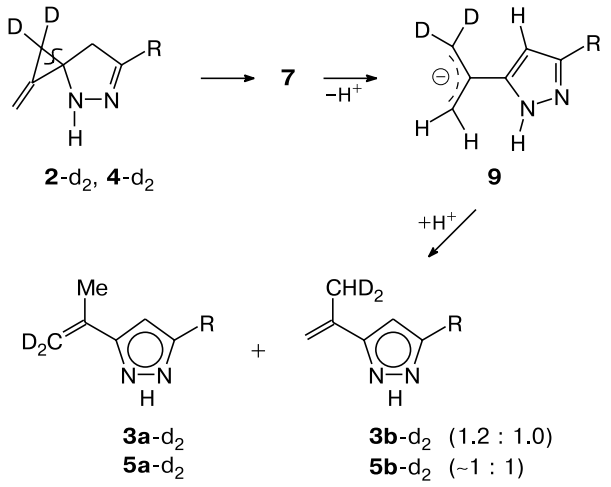
Decomposition of nitrosourea **6** under the action of K_2CO_3 in the presence of ethyl acrylate at 0 °C proceeds to completion in ~24 h giving rise to a mixture of spiro compound **4**-d_2 and pyrazole **5**-d_2 in ~1 : 1.5 ratio. According to ^{1}H NMR, after 2 h of the reaction, pyrazole **5**-d_2 can hardly be detected in the reaction mixture and the ratio of the starting urea **6** to the spiro[dihydropyrazolecyclopropane] **4**-d_2 formed amounts to ~4 : 1. These data demonstrate that the introduction of two deuterium atoms into the cyclopropane ring of spiro[dihydropyrazole-5,1′-cyclopropane] decreases substantially the rate of its isomerization into the corresponding isopropenylpyrazole, apparently, owing to increase in the stability of the CD_2—C_{spiro} bond in the methylidenecyclopropane fragment (the secondary isotope effect). After two days, the ^{1}H NMR spectrum exhibited mainly signals for pyrazole **5**-d_2, which was isolated by TLC in 44% yield. As in the case with acrylonitrile, both deuterium atoms were found either in the methylidene fragment (isomer **5a**-d_2) or in the methyl group (isomer **5b**-d_2), the ratio is ~1 : 1.

These results suggest a scheme of transformation that implies cleavage of the weakest C—C bond opposing the exocyclic double bond in the cyclopropane ring (Scheme 5). In our opinion, cleavage of the C—C bond to give zwitter-ion **7** is more likely, as this ion can readily lose a proton due to ring aromatization being thus converted into anion **9**. The intermediate formation of a zwitter-ion has been suggested previously for the transformations of methylidenecyclopropane spiro-fused with a 1,3-dioxane fragment.[7]

The intermediate formation of anion **9** is confirmed by the fact that in the isomerization carried out in a protic solvent, the isopropenyl group is formed due to proton abstraction from the solvent. For example, decomposition of *N*-(2-methylidenecyclopropyl)-*N*-nitrosourea on treatment with K_2CO_3 in CD_3OD at 0 °C in the presence of ethyl acrylate gives, after 1.5 h, mainly pyrazole **5**-d, containing, according to ^{1}H NMR data, one deuterium atom in the methyl group.* The spectrum exhibits a number of other distinct signals, which we assign to 1-methyl-

* Since the ^{1}H NMR spectrum was recorded in CD_3OD, deuterium exchange at the N—H bond was not taken into account.

Scheme 5



R = CN (**2**, **3**); COOEt (**4**, **5**)

idene-2-(trideuteriomethoxy)cyclopropane (**10**), formed apparently in the reaction of the methylidenecyclopropyldiazonium generated initially with excess CD_3OD (the ratio **5**-d : **10** ≈ 2.7 : 1).

Thus, the introduction of the exocyclic methylidene fragment into the three-membered ring of spiro[dihydropyrazole-5,1′-cyclopropanes] weakens the opposing bond and favors easy isomerization of these compounds into the corresponding isopropenylpyrazoles. The introduction of two deuterium atoms into the cyclopropane ring retards this transformation; after isomerization, both deuterium atoms are found either in the methyl or in the methylidene fragment of the isopropenyl substituent formed; this implies equivalence of the carbon atoms of the $=CH_2$ and $—CD_2—$ groups in the spiro-fused methylidenecyclopropane fragment during isomerization.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 (200.13 and 50.3 MHz) and Bruker AM-300 (300.13 and 75.5 MHz) spectrometers for solutions in $CDCl_3$, CD_2Cl_2, or CD_3OD containing 0.05% Me_4Si as the internal standard. *N*-(2-Methylidenecyclopropyl)-*N*-nitrosourea[1] and methylidenecyclopropane[8] were prepared by previously described procedures. DMSO-d_6 and CD_3OD with a deuterium content of at least 99.5% and freshly distilled acrylonitrile and ethyl acrylate (Merck) were used in experiments. 2,2,6,6-Tetramethylpiperidine was distilled *in vacuo* from $LiAlH_4$; Bu^tOK (Merck) was kept for 2 h at 100 °C (0.02 Torr) prior to use.

5(3)-Isopropenyl-3(5)-ethoxycarbonylpyrazole (5). Potassium carbonate (67 mg, 0.48 mmol) was added at 0 °C to a solution of *N*-(2-methylidenecyclopropyl)-*N*-nitrosourea (36 mg, 0.26 mmol) and ethyl acrylate (35 mg, 0.35 mmol) in 0.5 mL of CH_2Cl_2, and the mixture was stirred at this temperature for 2.5 h. Then the reaction mixture was filtered and the filtrate was concentrated *in vacuo* to give 38 mg of a yellow oily liquid. The ^1H NMR spectrum of the liquid exhibited strong signals for pyrazole **5** and signals for the methylene protons of the dihydropyrazole ring of spiro[dihydropyrazolecyclopropane] **4**, which formed an AB-system at δ 3.10 with the spin-spin coupling constant ^2J = 17.6 Hz. Preparative TLC (Silufol, ether—hexane (3 : 1)) gave 29 mg (62%) of pyrazole **5** as colorless crystals, R_f 0.58, m.p. 89—90 °C (*cf.* Ref. 3: b.p. 160 °C (1 Torr)). Found (%): C, 59.65; H, 6.89; N, 15,37. $C_9H_{12}N_2O_2$. Calculated (%): C, 59.99; H, 6.71; N, 15,55. ^1H NMR (200 MHz), $CDCl_3$, δ: 12.90 (br.s, 1 H, NH); 6.88 (s, 1 H, H(4)); 5.51 (quint., 1 H, $=CH_\alpha$, $^2J = {}^4J$ = 0.9 Hz); 5.15 (dq, 1 H, $=CH_\beta$, ^4J = 1.6 Hz, ^2J = 0.9 Hz); 4.38 (q, 2 H, OCH_2, J = 7.1 Hz); 2.13 (dd, 3 H, =CMe, ^4J = 0.9 Hz, ^4J = 1.6 Hz); 1.38 (t, 3 H, Me, J = 7.1 Hz). ^{13}C NMR (50.3 MHz), $CDCl_3$, δ: 161.0 (CO); 149.7 (C(5)); 139.7 (C(3)); 134.0 (=C); 113.3 ($=CH_2$); 105.5 (C(4)); 61.3 (OCH_2); 20.4 (=CMe); 14.1 (Me).

Study of deuterium exchange in methylidenecyclopropane on treatment with dimsylpotassium in DMSO-d_6. A suspension of KH in mineral oil (27 mg, ~35% w/w) was placed into an NMR tube under Ar. The suspension was washed with ether (4×0.4 mL) and the remaining ether was removed *in vacuo* to give ~9.3 mg (0.23 mmol) of KH. Then DMSO-d_6 (550 mg, 6.5 mmol) was added and the mixture was heated to 40 °C. After gas evolution ceased, methylidenecyclopropane (38 mg, 0.7 mmol) was added to the resulting light-brown solution and the tube was sealed. In the ^1H NMR spectrum recorded after 20 min, the ratio of the integral intensities of the signals for olefinic and cyclopropane protons was ~2 : 1, and after 2 h, this ratio was ~7 : 1, which was close to the equilibrium state. Distillation into another tube gave 32 mg (80%) of methylidenecyclopropane as a colorless liquid (the degree of deuteration ~93%). An increase in the time of storage of the reaction mixture (~20 h) resulted in a markedly lower yield of methylidenecyclopropane (15—20%).

2,2,3,3-Tetradeuterio(methylidene)cyclopropane. Potassium hydride (0.08 g, 2.0 mmol) prepared from a suspension of KH in mineral oil after washing with ether (4×7 mL) was placed in a 50-mL thick-walled tube with a magnetic stirring bar under Ar. DMSO-d_6 (10.1 g, 0.12 mol) was added with stirring and the mixture was heated to 40 °C. After gas evolution ceased, the tube was cooled to −50 °C, liquid methylidenecyclopropane (3.35 g, 60 mmol) was added, and the tube was sealed. Then it was heated to ~20 °C, the resulting solution was stirred for 2 h, and methylidenecyclopropane (~2.85 g) was distilled into a second tube containing a solution of dimsylpotassium (from KH (0.08 g, 2.0 mmol)) in DMSO-d_6 (10.9 g, 0.13 mol). After stirring for 2 h, the product was distilled into a cooled trap to give 2.33 g (68%) of 2,2,3,3-tetradeuterio(methylidene)cyclopropane as a colorless liquid. The deuterium content was ~95%. ^1H NMR (300 MHz), $CDCl_3$, δ: 5.41 (br.s, $=CH_2$) and 1.04 (m, CD_2—CHD), integral intensity ratio ~10 : 1. ^{13}C NMR (50.3 MHz), $CDCl_3$, δ: 131.0 (=C); 103.4 ($=CH_2$); 2.0 (quint., CD_2, J = 24.7 Hz).

1,3,3-Trideuterio-2-methylidenecyclopropanecarboxylic acid (8). ***A.*** A 1.95 *M* hexane solution of BuLi (15 mL, 29.3 mmol) was added with vigorous stirring at −50 °C over a period of 20 min to a solution of 2,2,3,3-tetradeuterio(methylidene)cyclopropane (1.85 g, 32 mmol) (deuterium content ~95%) in 25 mL of anhydrous THF. The reaction mixture was warmed to 0 °C, stirred for 1 h, and cooled to −80 °C. The resulting light-yellow solution was poured onto solid CO_2 and left for 16 h in an atmosphere of CO_2. The resulting slurry was diluted with 80 mL

of water and washed with ether (2×10 mL). The aqueous layer was acidified with HCl to pH 1 and extracted with ether (6×10 mL). After drying ($MgSO_4$) and removal of the ether, the residue was fractionated *in vacuo*. Fraction 1 (0.25 g) with b.p. 75—80 °C (11 Torr) was a mixture of valeric and deuterio(methylidene)cyclopropanecarboxylic acids in ~12 : 1 molar ratio. Fraction 2 (0.75 g) with b.p. 81—83 °C (11 Torr) was a mixture of the same acids in ~4 : 1 molar ratio.

B. A 1.95 *M* hexane solution of BuLi (66.7 mL, 0.13 mol) was added with stirring under Ar over a period of 45 min to a cooled (−95 °C) solution containing Bu^tOK (15.7 g, 0.14 mol) and 2,2,6,6-tetramethylpiperidine (18.4 g, 0.13 mol) in 85 mL of anhydrous THF. The temperature was maintained between −90 and −95 °C. Then the reaction mixture was warmed to −70 °C over a period of 40 min and stirred at this temperature for 15 min. The resulting yellow-orange suspension was cooled again to −85 °C and a solution of 2,2,3,3-tetradeuterio(methylidene)cyclopropane (~95%) (4.63 g, 0.08 mol) in 10 mL of anhydrous THF was rapidly added. The mixture became homogeneous and acquired a bright-orange color. The mixture was stirred for an additional 25 min, the temperature being gradually brought to −60 °C, then the mixture was cooled to −80 °C and the resulting solution was poured onto solid CO_2. This was accompanied by foaming and the reaction mixture became dark-red. After 12 h, ~280 mL of a 5% solution of KOH was added to the resulting thick orange material to bring pH to 10.5. The aqueous layer was washed with ether (2×45 mL), acidified with HCl to pH 1, and extracted with ether (6×25 mL). The organic fractions were washed with brine (2×25 mL) and dried with $MgSO_4$. After removal of the solvent, the residue was fractionated *in vacuo* to give 0.95 g (~12%) of trideuterio(methylidene)cyclopropanecarboxylic acid **8** as a colorless liquid, b.p. 87—90 °C (13 Torr). ^{1}H NMR (200 MHz), $CDCl_3$, δ: 10.90 (br.s, OH); 5.57 (br.s, 2 H, $=CH_2$); 2.25 (br.s, 0.13 H, residual proton at C(1)); 1.87, 1.70 (both br.s, по 0.12 H, residual protons at C(3)). ^{13}C NMR (50.3 MHz), $CDCl_3$, δ: 179.1 (COOH); 129.8 (C(2)); 105.1 ($=CH_2$); 17.4 (t, C(1), J = 26.0 Hz); 11.8 (quint, C(3), J = 12.7 Hz).

1,3,3-Trideuterio-2-methylidenecyclopropanecarboxylic acid chloride was prepared by a previously described procedure.[1] ^{1}H NMR (200 MHz, $CDCl_3$), δ: 5.69, 5.66 (both s, each 1 H, $=CH_2$); 2.71 (br.s, 0.13 H, residual proton at C(1)); 2.13, 1.90 (both br.s, each 0.12 H, residual protons at C(3)).

***N*-(1,3,3-Trideuterio-2-methylidenecyclopropyl)urea** was prepared by a previously described procedure.[1] ^{1}H NMR (200 MHz, CD_3OD), δ: 5.73, 5.54 (both br.s, each 1 H, $=CH_2$); 4.90 (br.s, NH and NH_2, overlapped with the signal of residual protons of the solvent); 3.10 (br.s, 0.13 H, residual proton at C(1)); 1.56, 1.15 (both br.s, each 0.13 H, residual protons at C(3)). ^{13}C NMR (50.3 MHz, CD_3OD), δ: 163.0 (CO); 133.3 (C(2)); 107.0 ($=CH_2$); 25.2 (t, C(1), J = 27.1 Hz); 13.2 (quint, C(3), J = 11.8 Hz).

Nitroso-*N*-(1,3,3-trideuterio-2-methylidenecyclopropyl)-*N*-urea (6) was prepared by a previously described procedure.[1] ^{1}H NMR (200 MHz, CD_3OD), δ: 5.88, 5.62 (both s, each 1 H, $=CH_2$); 4.93 (br.s, NH_2, overlapped with the signal of the residual protons of the solvent); 3.02 (br.s, 0.14 H, residual proton at C(1)); 1.88, 1.29 (both br.s, each 0.13 H, residual protons at C(3)). ^{13}C NMR (50.3 MHz, $CDCl_3$), δ: 154.6 (CO); 127.7 (C(2)); 110.4 ($=CH_2$); 24.1 (t, C(1), J = 28.1 Hz); 12.7 (quint, C(3), J = 12 Hz).

1,1-Dideuteriobutatriene. Sodium methoxide (6.5 mg, 0.12 mmol) was added at −50 °C to a solution of nitrosourea **6** (4.3 mg, 0.03 mmol) in 0.4 mL of CD_3OD containing 7.1 mg of *p*-dibromobenzene as an internal standard in an NMR tube. During slow warming-up of the sample, gas evolution was observed, which started at −20 °C. The reaction mixture was kept at −10 °C for 25 min until gas evolution completely ceased. Then an ^{1}H NMR spectrum was recorded. The ratio of integral intensities of the signals at δ 7.46 and δ 5.35 was ~2.6 : 1, which corresponded to the formation of butatriene-d_2 in ~80% yield (the degree of its deuteration was assumed to be the same as in the starting urea **6**).

Reaction of *N*-(1,3,3-trideuterio-2-methylidenecyclopropyl)-*N*-nitrosourea (6) with acrylonitrile. Potassium carbonate (13.8 mg, 0.1 mmol) was added at 0 °C under Ar to a solution of nitrosourea **6** (7.2 mg, 0.05 mmol) and acrylonitrile (4.4 mg, 0.08 mmol) in 0.4 mL of CD_2Cl_2 in an NMR tube. The reaction mixture was occasionally shaken, the temperature being maintained at 0 °C. According to ^{1}H NMR spectrum, nitrosourea completely decomposed after 24—25 h and the reaction mixture contained spiro compound **2**-d_2 and pyrazole **3**-d_2 in ~3.3 : 1 ratio. ^{1}H NMR spectrum for **2**-d_2 (300 MHz, CD_2Cl_2) δ: 6.20 (br.s, NH); 5.78, 5.64 (both br.s, each 1 H, $=CH_2$); 3.16, 3.06 (both d, each 1 H, H(7), ^2J = 17.1 Hz); 1.51 (br.s, 0.27 H, residual protons at C(3′)). The reaction mixture was filtered, the precipitate was washed with $CHCl_3$, the filtrate was concentrated, and the residue was dissolved in $CDCl_3$ and left for two days at 20 °C. According to ^{1}H NMR spectrum, isomerization of spiro[dihydropyrazolecyclopropane] into pyrazole was virtually complete. Preparative TLC gave 3.5 mg (52%) of cyanopyrazole **3**-d_2 as colorless crystals. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.10 (br.s, 1 H, NH); 6.68 (s, 1 H, H(4)); 5.51, 5.26 (both br.s, each ~0.5 H, $=CH_2$ ($=CD_2$)); 2.11 (br.s, 2.3 H, CHD_2 (CH_3)). For a degree of deuteration of ~87%, the ratio of isomers **3b** and **3a** with CHD_2 and $=CD_2$ fragments was ~45 : 55.

Reaction of *N*-methylidenecyclopropyl-*N*-nitrosoureas with ethyl acrylate. *A.* Potassium carbonate (13.8 mg, 0.1 mmol) was added at 0 °C to a solution of nitrosourea **6** (7.2 mg, 0.05 mmol) and ethyl acrylate (7.5 mg, 0.075 mmol) in 0.4 mL of CD_2Cl_2 in an NMR tube. The reaction mixture was occasionally shaken, the temperature being maintained at 0 °C. After 2 h, an ^{1}H NMR spectrum was recorded. According to this spectrum, the reaction mixture contained the starting nitrosourea **6** and spiro[dihydropyrazolecyclopropane] **4**-d_2 in ~4 : 1 ratio (based on the ratio of integral intensities of the olefinic protons in **6** and the methylene protons of the pyrazoline ring in **4**-d_2). After 24 h at 0 °C, apart from traces of the initial nitrosourea **6**, the reaction mixture contained spiro[dihydropyrazolecyclopropane] **4**-d_2 and pyrazole **5**-d_2 in ~1 : 1.5 ratio. The mixture was kept at 20 °C for an additional 24 h and filtered. The precipitate was washed with $CHCl_3$, the filtrate was concentrated, and the residue was purified by TLC (as above) to give 4.0 mg (44%) of crystalline pyrazole **5**-d_2. ^{1}H NMR (200 MHz, $CDCl_3$), δ: 7.10 (br.s, 1 H, NH); 6.88 (s, 1 H, H(4)); 5.52, 5.16 (both br.s, each 0.56 H, $=CH_2$ ($=CD_2$)); 4.38 (q, 2 H, OCH_2, J = 7.1 Hz); 2.13 (br.s, 2.2 H, CHD_2 (CH_3)); 1.38 (t, 3 H, Me, J = 7.1 Hz). For a degree of deuteration of ~87%, the ratio of isomers **5b** and **5a** with CHD_2 and $=CD_2$ fragments was ~1 : 1.

B. Potassium carbonate (21.1 mg, 0.15 mmol) was added at 0 °C to a solution containing *N*-methylidenecyclopropyl-*N*-nitrosourea (9.9 mg, 0.07 mmol) and ethyl acrylate (13 mg,

0.13 mmol) in 0.4 mL of CD_3OD in an NMR tube. The reaction mixture was shaken at some intervals for 1.5 h, the temperature being maintained at 0 °C. According to ^1H NMR spectrum, in addition to excess ethyl acrylate, the reaction mixture contained spiro[dihydropyrazolecyclopropane] **4** (identified based on the H(4) proton signals at δ 3.10, AB-system, ^2J = 17.6 Hz), pyrazole **5**, and 1-methylidene-2-(trideuteriomethoxy)cyclopropane (**10**) in ~1 : 15 : 5.5 ratio. ^1H NMR spectrum for **10** (300 MHz, CD_3OD), δ: 5.66 (dt, 1 H, $=CH_\alpha$, ^4J = 2.8 and 1.3 Hz); 5.61 (q, 1 H, $=CH_\beta$, $^4J \approx$ 2.1 Hz); 3.87 (dddd, 1 H, H(1), J_{cis} = 7.8 Hz, J_{trans} = 3.6 Hz, ^4J = 2.8 and 1.3 Hz); 1.85 (dddd, 1 H, H(3α), ^2J = 10.3 Hz, J_{cis} = 7.8 Hz, ^4J = 2.8 and 2.1 Hz); 1.71 (dddd, 1 H, H(3β), ^2J = 10.3 Hz, J_{trans} = 3.6 Hz, ^4J = 2.8 and 2.1 Hz) (see Ref. 9). Then the reaction mixture was filtered and the filtrate was concentrated *in vacuo* (to remove the solvent, excess ethyl acrylate and compound **10**). The residue was dissolved in 0.7 mL of ether, washed with water, dried with $MgSO_4$, and concentrated *in vacuo* to give 7.3 mg (58%) of crystalline 5(3)-[1-(deuteriomethyl)vinyl]-3(5)-ethoxycarbonylpyrazole (**5**-d). The ^1H and ^{13}C NMR spectra were similar to those presented above for pyrazole **5** except for the signals for the CH_2D group at the double bond manifested at δ 2.11 (ddt, 2 H, ^4J = 1.0 Hz, ^4J = 1.6 Hz, J_{H-D} = 2.2 Hz) and δ 20.4 (t, J = 19.4 Hz), respectively.

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