Mendeleev Commun., 1997, 7(5), 200–201

The first example of the generation and trapping of diazospiropentane by unsaturated compounds

Yury V. Tomilov,* Evgeny V. Shulishov, Galina P. Okonnishnikova and Oleg M. Nefedov*

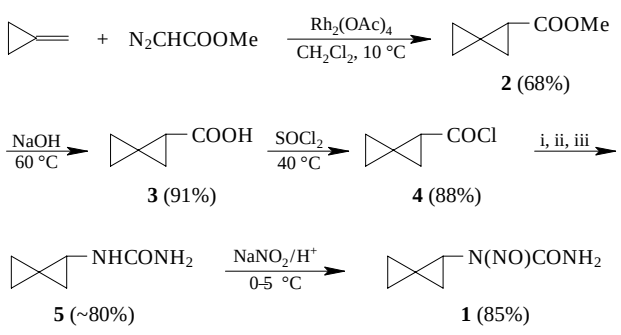
N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation.
Fax: +7 095 135 5328

Alkaline hydrolysis of *N*-spiropentyl-*N*-nitrosourea at –50 °C generates unknown diazospiropentane *in situ*, which is trapped with methyl methacrylate or 3,3-dimethylcyclopropene yielding the corresponding 1-pyrazolines with a spiropentane fragment in the molecule. Some chemical transformations of the products obtained are performed.

Alkaline decomposition of *N*-cyclopropyl-*N*-nitrosourea is supposed to proceed with intermediate formation of diazocyclopropane and/or cyclopropylidene which can be trapped with appropriate olefins. So, in the presence of several methylenecyclopropanes strained polyspirocyclopropanes[1–3] are formed as a result of carbene addition to the double bond. Under the same conditions unsaturated substrates containing a strained endocyclic double bond[4,5] or a double bond conjugated with an electron-withdrawing group[6–9] easily react with diazocyclopropane generated *in situ* yielding spiro(cyclopropanepyrazolines) as 1,3-dipolar cycloaddition products. The generation and trapping of spirocyclopropane homologues of diazocyclopropane to obtain the corresponding polyspirocyclopropanepyrazolines are not known.

In the present study, we carried out for the first time alkaline hydrolysis of *N*-nitroso-*N*-spiropentylurea **1** in the presence of 3,3-dimethylcyclopropene or methyl methacrylate and investigated some chemical transformations of the adduct prepared from diazospiropentane generated *in situ* and methyl methacrylate. The starting nitrosourea **1** was synthesised in several steps, similarly to the preparation of other *N*-cyclopropyl-*N*-nitrosoureas. Methoxycarbonylcyclopropanation of methylenecyclopropane with 1/5 equiv. of methyl diazoacetate in the presence of dirhodium tetraacetate gave methyl spiropentylcarboxylate **2** in 68% yield. Hydrolysis of the ester **2** and interaction of the acid **3** thus formed with thionyl chloride afforded acid chloride **4** (in a yield of ~80% over two steps). Compound **4** was then converted into spiropentylurea **5** (~80%) *via* non-isolated spiropentanoyl azide and spiropentane isocyanate. The structure and satisfactory purity of the product were confirmed by ^{1}H NMR spectroscopy. Nitrosourea **1** was obtained in 85% yield by nitrosation of the urea **5** with aqueous $NaNO_2$ at 0–5 °C in acid solution by the standard procedure; the precipitate was filtered and dried *in vacuo* (Scheme 1).

The crucial step – the *in situ* generation and trapping of diazospiropentane **6** – was accomplished by the addition of solid sodium methoxide to a stirred solution of the nitrosourea **1** and unsaturated compound in methanol (molar ratio 1.5:1:1.5) maintained at –5 0 °C. After that, the reaction mixture was allowed to warm up to 20 °C, diluted with water and extracted with dichloromethane. Thus, the reaction



Scheme 1 *Reagents and conditions*: i, NaN_3 (H_2O–acetone); ii, toluene, 90 °C; iii, NH_3 (dry).

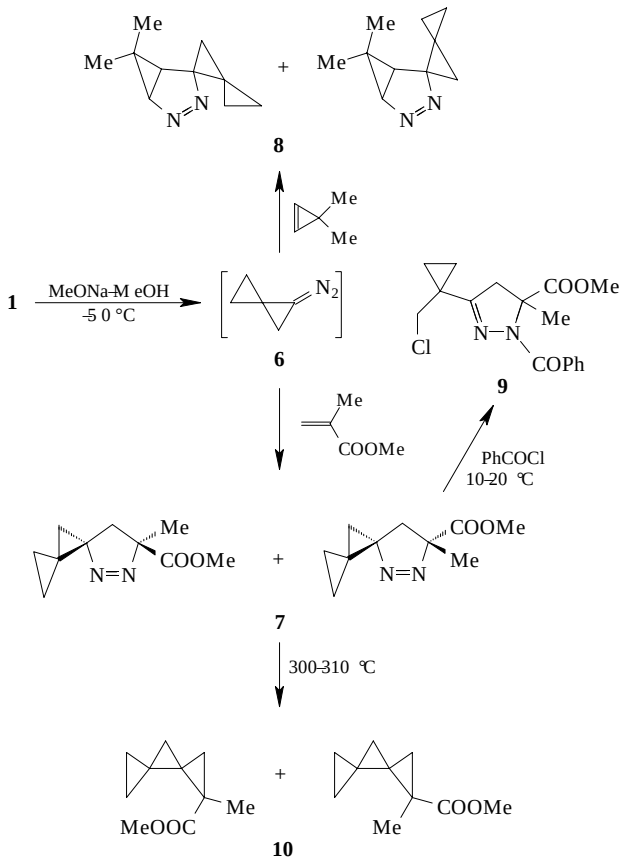
of **6** with methyl methacrylate proceeds as a 1,3-dipolar cycloaddition and gives two isomeric 8-methoxycarbonyl-8-methyl-6,7-diazadispiro[2.1.4.0]non-6-enes **7** in a total yield of 72% (ratio ~1:1). At higher temperatures (for example at –20 °C) the total yield of pyrazolines **7** decreased significantly (~20%). However, products corresponding to carbene addition to methyl methacrylate were not detected. ^{1}H and ^{13}C NMR spectra† of **7** contain a double set of signals, the positions and multiplicities of which are similar to those of the signals of 3′-methoxycarbonyl-3′-methylspiro(cyclopropane-1,5′-pyrazoline-1′) obtained previously by the addition of diazocyclopropane generated *in situ* to methyl methacrylate.[6] In both isomers of pyrazoline **7**, the methylene protons of the pyrazoline ring are manifested as a doublet with ^2J = 12.7 Hz, while the methylene protons of the tetrasubstituted cyclopropane ring account for a doublet with ^2J = 5.1 Hz. Unfortunately, the data available at present do not permit reliable assignment of the signals to particular isomers.

Similarly, the *in situ* generation of diazospiropentane **6** followed by its trapping with 3,3-dimethylcyclopropene gives rise to the corresponding bicyclic pyrazoline **8** (yield ~35%) with a spiropentane fragment. The product is formed as a mixture of two isomers in a ratio of ~1.1:1, according to the ^{1}H NMR spectrum. The low yield of the pyrazoline **8** in this case is surprising, because previously, 3,3-dimethylcyclopropene had been shown to be an effective trapping reagent for diazocyclopropane and its dimethyl and dichloro derivatives,[1,10] generated *in situ* at temperatures –30 to 0 °C and giving (exceptionally) the corresponding 1-pyrazolines.

The compounds prepared are sufficiently stable under ambient conditions and were purified by TLC (silica gel, ether–hexane 4:1) without separation of pure isomers (Scheme 2).

Recently,[11] we have shown that interaction of acyl halides with the conjugated azocyclopropane system proceeds as 1,5-addition accompanied by opening of the cyclopropane ring. Now we have found that a similar reaction of the pyrazoline **7** (a ~1:1 mixture of isomers) with an equimolar quantity of benzoyl chloride in a CH_2Cl_2 solution at 10–20 °C also occurs with high selectivity and gives the corresponding 1-benzoyl-3-(1′-chloromethylcyclopropyl)-2-pyrazoline **9** in a high yield. Opening of the tetrasubstituted cyclopropane ring in both isomers of the pyrazoline **7** affords compound **9** as the only product, as indicated by the data of both ^{1}H and ^{13}C NMR spectra.

Pyrolysis of spiro(1-pyrazoline-5,1′-spiropentane) **7** occurs without opening of the cyclopropane ring, although it is carried out at a high temperature. In fact, when the pyrazolines **7** (a ~1:1 mixture of isomers) mixed with benzene is passed through a quartz tube with quartz packing at ambient pressure and at 300–315 °C, 1-methoxycarbonyl-1-methyldispiro[2.1.2.0]heptane **10** is formed in ~90% isolated yield. The structure of the compound obtained was confirmed by satisfactory results of elemental analysis and by spectral data. The ^{1}H and ^{13}C NMR spectra† of this product exhibit a double set of signals corresponding to two isomers of dispiroheptane **10** present in a ratio ~1.4:1. No signals are recorded in the olefinic regions of the spectra.



Scheme 2

Pyrolytic elimination of nitrogen from pyrazolines **8** at temperature 290 °C proceeds in 92% conversion, but unlike **7** gives a very complicated mixture of hydrocarbons.

These results show that alkaline decomposition of *N*-nitroso-*N*-spiropentylurea involves the intermediate formation of diazospiropentane, which can be trapped with double bonds as 1,3-dipolar cycloaddition adducts. Pyrolysis of 1-pyrazoline prepared from diazospiropentane and methyl methacrylate proceeds with high selectivity and can serve as a convenient method for the preparation of functionally substituted dispiroheptanes.

The authors thank the Russian Foundation for Basic Research for financial support (grant no. 96-03-33035).

References

1 L. Fitjer and J.-M. Conia, *Angew. Chem.*, 1973, **85**, 349.
2 S. Zð lner, H. Buchholz, R. Boese, R. Gleiter and A. de Meijere, *Angew. Chem.*, 1991, **103**, 1544.
3 S. I. Kozhushkov, T. Haumann, R. Boese and A. de Meijere, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 401 and literature cited therein.
4 Yu. V. Tomilov, E. V. Shulishov and O. M. Nefedov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 1057 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 939).
5 Yu. V. Tomilov, E. V. Shulishov, G. P. Okonnishnikova, and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2199 (*Russ. Chem. Bull.*, 1995, **44**, 2105).
6 (*a*) P. Bladon and D. R. Rae, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2240; (*b*) P. Bladon and D. R. Rae, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2460.
7 P. Bladon, D. R. Rae and A. D. Tait, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1468.
8 Yu. V. Tomilov, E. V. Shulishov, I. V. Kostyuchenko and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 532 (*Russ. Chem. Bull.*, 1997, **46**, 511).
9 Yu. V. Tomilov, E. V. Shulishov, S. A. Yarygin and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2203 (*Russ. Chem. Bull.*, 1995, **44**, 2109).
10 Yu. V. Tomilov, E. V. Shulishov, I. P. Klimenko and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2698 (*Russ. Chem. Bull.*, 1996, **45**, 2557).
11 Yu. V. Tomilov, G. P. Okonnishnikova, E. V. Shulishov and O. M. Nefedov, *Mendeleev Commun.*, 1994, 119.

† Compound **7**: bp 100–103 °C (0.5 Torr), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.82 and 3.72 (two s, OMe), 2.38 and 1.51 (two d, CH_2-6 in one isomer, ^2J 12.7 Hz), 2.12 and 1.70 (two d, CH_2-6 in the other isomer, ^2J 12.7 Hz), 2.32 and 1.53 (two d, CH_2-4 in one isomer, ^2J 5.1 Hz), 2.32 and 1.55 (two d, CH_2-4 in the other isomer, ^2J 5.1 Hz), 1.42 and 1.67 (two s, Me), 1.22, 1.08, 0.86 and 0.76 (m, CH_2CH_2 in both isomers). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 171.7, 171.3 (COO), 92.4, 92.1 (C-7), 74.3, 73.8 (C-5), 52.8, 52.7 (OMe), 34.6, 34.3 (C-6), 22.4, 22.1 (Me), 21.8, 22.0 (C-3), 20.3, 20.0 (C-4), 6.6, 6.7 and 4.0, 4.3 (C-1 and C-2).

Compound **8**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.60 and 4.50 (two d, CH-1, ^3J 5.0 Hz), 2.26 and 1.38 (two d, CH_2-3′ in one isomer, ^2J 4.7 Hz), 2.22 and 1.78 (two d, CH_2-3′ in the other isomer, ^2J 4.7 Hz), 1.53 and 1.40 (two d, CH-5, ^3J 5.0 Hz), 1.15 and 1.16 (two s, *anti*-Me), 0.70–1.30 (m, CH_2CH_2 in both isomers), 0.42 and 0.73 (two s, *syn*-Me). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 75.7, 75.4 (C-1), 73.8, 72.8 (C-4), 23.9, 24.0 (*anti*-Me), 23.4, 17.6 (C-3′), 22.7, 22.2, 22.0 and 19.1 (C-6, C-2′), 13.5, 13.4 (*syn*-Me), 6.2, 6.1 and 6.0, 3.7 (C-2′′ and C-3′′).

Compound **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.92 and 7.39 (two m, 2+3H, C_6H_5), 3.73 (s, 3H, OMe), 3.67 (s, 2H, CH_2Cl), 3.13 and 2.74 (two d, 1+1H, CH_2-4, ^{2}J 17.5 Hz), 1.74 (s, 3H, CH_3), 1.18 and 1.01 (two m, 2+2H, CH_2CH_2). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 171.7 (COO), 165.3 (NCO), 157.2 (C-3), 133.6 (*ipso*-C in Ph), 130.8 (*p*-C), 129.8 (*o*-C), 127.3 (*m*-C), 67.0 (C-5), 52.6 (OMe), 49.4 (CH_2Cl), 45.6 (C-4), 23.6 (C in cyclo-C_3H_4), 21.3 (Me), 15.2 and 14.7 (CH_2CH_2). MS, *m*/*z*: 336 and 334 (0.9 and 2.4) $[M]^+$, 299 (9) $[M–Cl]^+$, 277 and 275 (3 and 9) $[M–COOMe]^+$, 231 and 229 (2.6 and 8) $[M–COPh]^+$, 105 (100) $[COPh]^+$.

Compound **10**: bp 85–90 °C (30 Torr), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.67 and 3.57 (two s, OMe), 1.73 and 1.61 (two d, *cis*-H-2, ^2J 3.9 Hz), 1.30, 1.21, 1.20 and 1.10 (four d, CH_2-4 in both isomers, ^2J 3.9 Hz), 0.91 and 1.08 (two d, *trans*-H-2, ^2J 3.9 Hz), 0.7–0.9 (m, CH_2CH_2 in both isomers). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 175.4, 175.6 (COO), 51.7, 51.3 (OMe), 28.3, 29.2 (C-1), 25.5, 24.2 (C-3), 21.3, 21.2 (C-2), 16.8, 17.6 (Me), 14.6, 15.1 (C-5), 12.9, 10.5 (C-4), 5.1, 5.3 and 4.0, 4.1 (C-6 and C-7). MS, *m*/*z*: 165 (2.5) $[M–H]^+$, 151 (16) $[M–Me]^+$, 135 (7) $[M–OMe]^+$, 107 (69) $[M–COOMe]^+$, 91 (100) $[C_7H_7]^+$.

Received: Moscow, 29th May 1997
Cambridge, 17th July 1997; Com. 7/03878J