Unusual reaction of aziridine dimer with acetylene dicarboxylates

Remir G. Kostyanovsky,*[a] Yurii I. El'natanov,[a] Ivan I. Chervin,[a] Mikhail Yu. Antipin[b] and Konstantin A. Lyssenko[b]

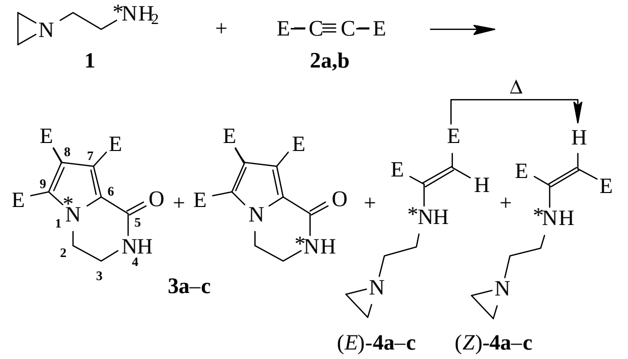
[a] *N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 117977 Moscow, Russian Federation. Fax: +7 095 938 2156*

[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 117813 Moscow, Russian Federation. Fax: +7 095 135 5085*

The 1-(2-aminoethyl)aziridine (aziridine dimer) 1 reacts with acetylene dicarboxylates to give 1,4-diaza-5-oxobicyclo[4.3.0]nonanes (7-azaindolizines) 3 together with the usual enamine adducts 4; the product structures are confirmed spectroscopically and, in the 3 also by X-ray diffraction and by an independent synthesis from furan 5.

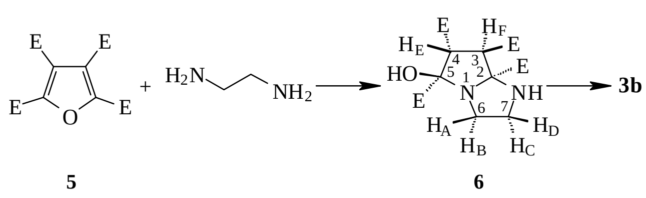
Treatment of the aziridine dimer **1**[1] and the terminally labelled dimer **1**-$^{15}NH_2$[†] with acetylene dicarboxylates **2a,b** afforded the 7,8,9-tris(alkoxycarbonyl)-1,4-diaza-5-oxobicyclo[4.3.0]nonanes **3a–c**, along with the usual adducts (*E*)- and (*Z*)-**4a–c** (Scheme 1).

The structures of **3,4** were confirmed spectroscopically[‡] (Figure 1). The structure of **3a** was also confirmed by X-ray diffraction[§] (Figure 2) and also by an independent synthesis of **3b** from furan **5**[3,‡] (Scheme 2). The formation of **3a,b** which is also accompanied by ethylene elimination and ^{15}N label randomization can be explained by the transformations indicated in Scheme 3. The key stages of the proposed mechanism are confirmed by the known easy ethylene



a E = CO_2R, *N = ^{14}N, R = Me
b E = CO_2R, *N = ^{14}N, R = Et
c E = CO_2R, *N = ^{15}N, R = Et

Scheme 1



E = CO_2Et

Scheme 2

[†] NMR spectra were recorded at 400 MHz (^{1}H) and 100.61MHz (^{13}C). The aziridine dimer **1**-^{15}N was prepared by the reduction of aziridinoacetamide-$^{15}NH_2$ ($LiAlH_4$ in boiling THF, 12h), yield 12.3%, bp 127 °C; ^{1}H NMR ($CDCl_3$): δ 1.13 (m) and 1.72 (m) (2×2H, CH_2 ring), 1.43 (br. s, 2H, HN), 2.26 (dt, 2H, α-CH_2, $^{3}J_{HH}$ 5.8, $^{3}J_{HN}$ 2.1Hz) and 2.85 (dt, 2H, β-CH_2, $^{2}J_{HN}$ 0.9Hz); ^{13}CNMR ($CDCl_3$): δ 26.6 (dd, CH_2 ring, ^{1}J 163.7 and 173.4 Hz), 41.79 (ddt, β-CH_2, ^{1}J 133.2, ^{2}J 2.8, $^{1}J_{CN}$ 4.2 Hz) and 64.36 (dt, α-CH_2, ^{1}J 133.2, $^{2}J_{CN}$ 1.4 Hz). The starting material aziridinoacetamide-$^{15}NH_2$ was prepared from ethyl aziridinoacetate[2] by amidation with $^{15}NH_3$ (90% of ^{15}N) in MeOH–MeONa, 7days at 20°C; yield 89.4%, mp 88 °C; ^{1}HNMR ($CDCl_3$): δ 1.27 (m) and 1.84 (m) (2×2H, CH_2 ring), 2.90 (s, CH_2CO) and 6.72 (2H, $H_AH_B{}^{15}N$, ABX spectrum, $\Delta\nu$ =200, $^{2}J_{AB}$ 4.3, $^{1}J_{BX}$ 89.5, $^{1}J_{BX}$ 90.3Hz); ^{13}C {^{1}H} NMR ($CDCl_3$): δ 27.4 (s, CH_2 ring), 63.4 (d, CH_2CO, $^{2}J_{CN}$ 5.6 Hz) and 173.0 (d, CO, $^{1}J_{CN}$ 15.3Hz).

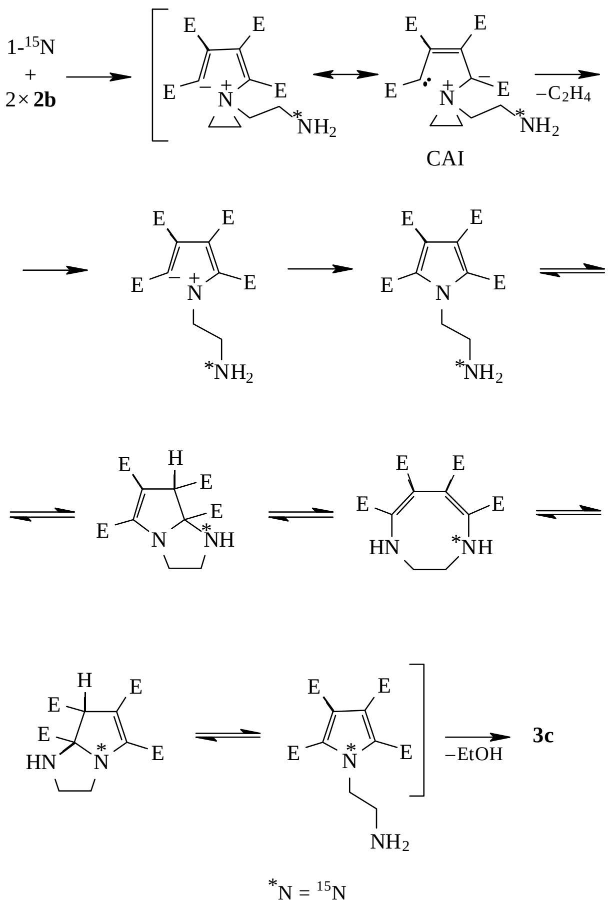
[‡] *Spectroscopic data for* **3a**: obtained from **1** and **2a** in Et_2O at 20 °C, 1h; yield 19.1%, mp188–189°C. Found: C, 50.41; H, 4.48; N, 9.12. Calc. for $C_{13}H_{14}N_2O_7$: C, 50.32; H, 4.55; N, 9.03%. ^{1}HNMR ([$^{2}H_8$]toluene): δ 2.73 (m, 2H, 3-CH_2), 3.62 (m, 2H, 2-CH_2), 3.54 (s), 3,62 (s) and 3.71 (s) (3×3H, MeO), and 7.30 (br.s, 1H, HN); ^{13}C NMR ([$^{2}H_6$]DMSO): δ 38.52 (t, 3-CH_2N, ^{1}J 141.0 Hz), 43.65 (2-CH_2, ^{1}J 146.4 Hz), 51.56 (q), 52.05 (q) and 52.36 (q) (3MeO, ^{1}J 147.7Hz), 118.3 (s), 119.2 (s) (7- and 8-C), 122.64 (s, 9-C) and 125.58 (dt, 6-C, $^{3}J_{CNCH}$ 2.7, $^{3}J_{CCNH}$ 5.6Hz), 156.81 (q, 5-C, $^{2}J = {}^{3}J$ = 4.2 Hz), 159.32 (q), 162.88 (q) and 163.29 (q) (CO_2Me, ^{3}J 4.2Hz); MS (EI, 70 eV, 240 °C): *m*/*z* (%): 310 (34.3) [M^+], 280 (15), 279 (100), 59 (13.2).

For **3b**: obtained from **1** and **2b** in Et_2O at 20 °C, 18 h, yield 31%, or quantitatively from **6** in [$^{2}H_8$]toluene in a sealed tube at 140 °C, 1h; mp140–141°C. Found: C, 54.62; H, 5.68; N, 8.10. Calc. for $C_{16}H_{20}O_7N_2$: C, 54.54; H, 5.72; N 7.95%. ^{1}H NMR ([$^{2}H_8$]toluene): δ 1.08 (t), 1.13 (t) and 1.21 (t) (3×3H, Me, ^{3}J 7Hz), 2.47 (br. m, 2H, 3-CH_2), 3.53 (br.m, 2H, 2-CH_2), 4.07 (q), 4.19 (q) and 4.33 (q) (3×2H, 3CH_2O) and 7.41 (br. s, 1H, HN); ^{13}C NMR (CD_3OD): δ 14.32 (q, 2Me, ^{1}J 126.2 Hz), 14.38 (Me, ^{1}J 127.4Hz), 40.43 (tt, 3-CH_2, ^{1}J 142.9, ^{2}J 2.8 Hz), 45.14 (tt, 2-CH_2, ^{1}J 147.0, ^{2}J 2.8 Hz), 62.64 (tq, 2CH_2O, ^{1}J 148.4, ^{2}J 4.2 Hz), 62.9 (tq, CH_2O, ^{1}J 148.2, ^{2}J 4.2 Hz), 120.79 (s), 122.65 (s) and 124.6 (s) (9-, 7-, 8-C), 127.02 (m, 6-C, ^{3}J 2.8 Hz), 159.96 (t, 5-C, ^{2}J 4.2 Hz), 160.73 (m), 165.11 (m) and 165.15 (m) (CO_2Et, ^{3}J 4.2 Hz).

For **3c**: yield 12.1%, mp 143–144 °C (Pr^iOH); ^{1}H NMR ([$^{2}H_8$]toluene): 1.09 (t), 1.14 (t) and 1.23 (t) (3×3H, 3Me, ^{3}J 7.0Hz), 2.45 (br. m, 2H, 3-CH_2, $^{2}J_{HN}$ 1.8 Hz), 3.5 (br.m, 2H, 2-CH_2, $^{3}J_{HN}$ 2.1Hz), 4.08 (q), 4.20 (q) and 4.33 (q) (3×2H, 3CH_2O) and 6.65 (d, 1H, HN, $^{1}J_{HN}$ 91.6Hz); ^{13}C NMR (CD_3OD): 14.31 (q, 2Me, ^{1}J 126.2Hz), 14.42 (Me, ^{1}J 127.4Hz), 40.43 (ttd, 3-CH_2, ^{1}J 142.9, $^{2}J_{CH}$ 2.8, $^{1}J_{CN}$ 8.4Hz), 45.14 (ttd, 2-CH_2N, ^{1}J 147.0, $^{2}J_{CH}$ 2.8, $^{1}J_{CN}$ 7.7Hz), 62.61 (tq), 62.62 (tq) and 62.9 (tq) (3CH_2O, ^{1}J 148.2Hz), 120.8 (dd, 7-C, $^{2}J = {}^{3}J_{CN}$ =2.9Hz), 122.63 (d, 8-C, $^{2}J_{CN}$ 4.2 Hz), 124.58 (d, 9-C, $^{1}J_{CN}$ 14.6Hz), 126.96 (d, 6-C, $^{1}J_{CN}$ 4.5Hz), 159.93 (d, 5-C, $^{1}J_{CN}$ 16.7Hz), 160.73 (m), 165.08 (m) and 165.14 (m) (CO_2Et, ^{3}J 4.2 Hz).

For **4a**: (*Z* : *E*, 3:1), yield 36.3%. For (*Z*)-**4a**: ^{1}H NMR ($CDCl_3$): δ 1.12 (m) and 1.75 (m) (4H, 2CH_2 ring), 2.34 (t, 2H, α-CH_2, ^{3}J 6.0Hz), 3.53 (td, β-CH_2, $^{3}J_{HCNH}$ 6.0 Hz), 3.65 (s) and 3.81 (s) (2×3H, 2MeO), 5.07 (s, 1H, HC=), 8.31 (br.s, 1H, HN). For (*E*)-**4a**: ^{1}H NMR ($CDCl_3$): δ 1.15 (m) and 1.74 (m) (4H, 2CH_2 ring), 2.41 (t, 2H, α-CH_2, ^{3}J 6.0Hz), 3.13 (td, 2H, β-CH_2, $^{3}J_{HCNH}$ 6.0 Hz), 3.62 (s) and 3.86 (s) (2×3H, 2MeO), 4.64 (s, 1H, HC=) and 5.3 (br. s, 1H, HN).

For **4b, 4c**: (*Z* : *E*, 1.2 : 1), yields 27%. (*Z*)-**4b**: ^{1}H NMR ($CDCl_3$): δ 1.12 (m) and 1.74 (m) (4H, 2CH_2 ring), 1.24 (t) and 1.34 (t) (2×3H, 2Me, ^{3}J 7.0 Hz), 2.34 (t, 2H, α-CH_2, ^{3}J 6.1 Hz), 3.53 (td, β-CH_2, $^{3}J_{HCNH}$ 6.1Hz), 4.07 (q) and 4.25 (q) (2×2H, 2CH_2O), 5.05 (s, 1H, HC=), 8.30 (br.s, 1H, HN). (Z)-**4c**: ^{1}H NMR ($CDCl_3$): δ 1.12 (m) and 1.74 (m) (4H, 2CH_2 ring), 1.24 (t) and 1.33 (t) (2×3H, 2Me, ^{3}J 7.0 Hz), 2.34 (dt, 2H, α-CH_2, $^{3}J_{HH}$ 6.1, $^{3}J_{HN}$ 2.8 Hz), 3.53 (tdd, 2H, β-CH_2, $^{2}J_{HCN}$ *ca.* 1, $^{3}J_{HCNH}$ 6.1Hz), 4.08 (q) and 4.24 (q)(2×2H, 2CH_2O), 5.04 (d, 1H, HC=, $^{3}J_{HN}$ 4.0 Hz) and 8.26 (dt, 1H, HN, $^{1}J_{HN}$ 90.4 Hz). (*E*)-**4b**: ^{1}H NMR ($CDCl_3$): δ 1.16 (m) and 1.74 (m) (4H, 2CH_2 ring), 1.23 (t) and 1.33 (t) (2×3H, 2Me, ^{3}J 7.0Hz), 2.41 (t, 2H, α-CH_2, ^{3}J 6.0 Hz), 3.13 (td, β-CH_2, $^{3}J_{HCNH}$ 6.0 Hz), 4.10 (q) and 4.30 (q) (2×2H, 2CH_2O), 4.64 (s, 1H, HC=) and 5.09 (br.s,1H, HN). (*E*)-**4c**: ^{1}H NMR ($CDCl_3$): δ 1.15 (m) and 1.74 (m) (4H, 2CH_2 ring), 1.23 (t) and 1.35 (t) (2×3H, 2Me, ^{3}J 7.0Hz),



Scheme 3

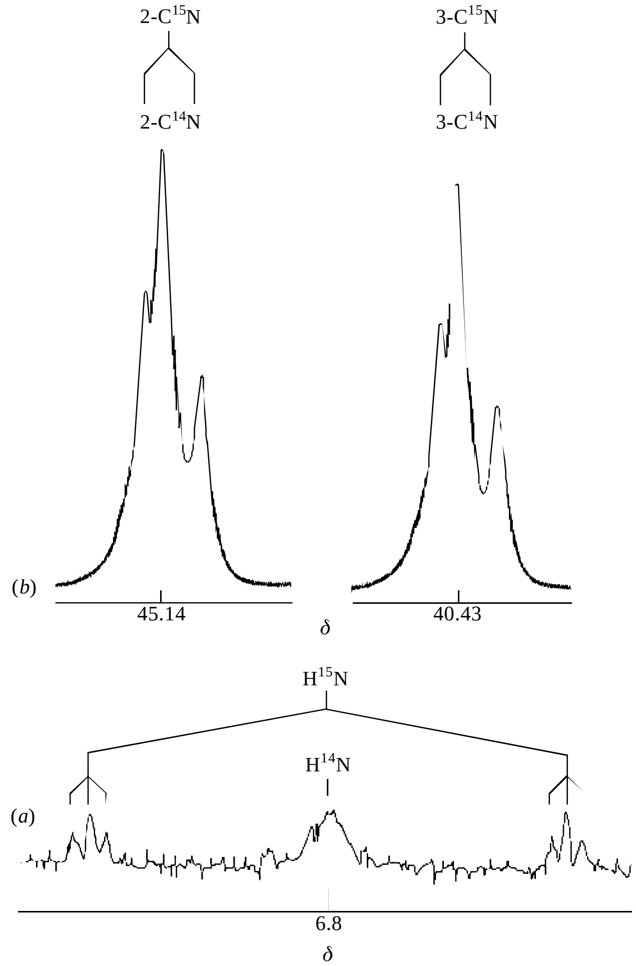


Figure 1 (*a*) ^{1}H NMR spectrum of the 4-NH proton of **3c** and (*b*) ^{13}C {^{1}H} NMR spectrum of the 2-C and 3-C carbon atoms of **3c**.

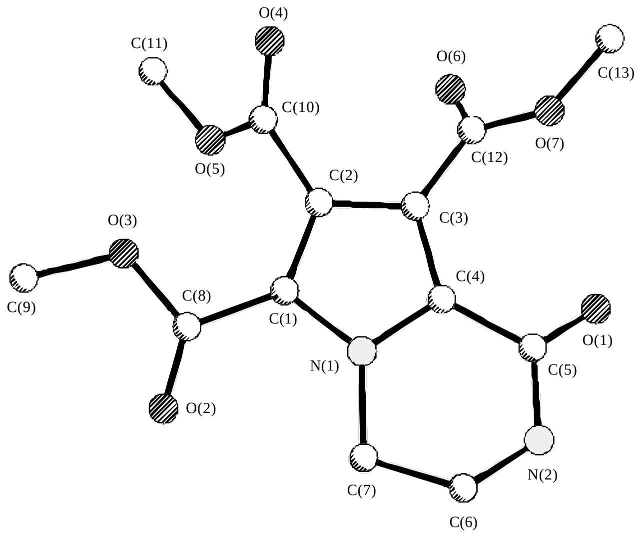


Figure 2 Crystal structure of **3a**. Selected bond lengths (Å) and angles (°): N1–C1 1.383(6), C1–C2 1.385(6), C2–C3 1.401(6), C3–C4 1.402(6), C4–N1 1.373(6), C4–C5 1.477(6), C5–N2 1.347(6), N2–C6 1.459(7), C6–C7 1.509(7), C7–N1 1.476(5); C1N1C4 109.7(3), N1C1C2 106.7(4), C1C2C3 109.2(4), C2C3C4 106.5(4), C3C4N1 107.9(4), C4N1C7 122.5(4), N1C4C5 120.2(4), C4C5N2 114.6(4), C5N2C6 122.6(4), N2C6C7 111.6(4), C6C7N1 107.7(4), C1N1C7 127.8(4), C3C4C5 131.3(4).

elimination from aziridinium ylides[4] [the first intermediate zwitterion in Scheme 3 can be represented as a mesomeric form of carbenaziridinium ylide (CAI)] and by the isolation of the intermediate **6** before the lactamization in **3b** (Scheme 2).

This work was accomplished with financial support from

2.41 (br. m, 2H, α-CH$_2$, 3.12 (tdd, β-CH$_2$, $^2J_{\mathrm{HCNH}}$ 6.1 Hz), 4.10 (q) and 4.29 (q) (2×2H, 2CH$_2$O), 4.62 (d, 1H, HC=, $^3J_{\mathrm{HN}}$ 1.5 Hz), 5.37 (dt, 1H, HN, $^1J_{\mathrm{HN}}$ 93Hz).

Furan **5**, under the action of ethylene-1,2-diamine in toluene (14 days, 20°C) gave intermediate **6**. The latter was isolated by gradient chromatography (silica gel, heptane–ethyl acetate, 0→ 60%), yield 24%, colourless oil. Found: C, 52.10; H, 6.69; N, 6.82. Calc. for $C_{18}H_{28}N_2O_9$: C, 51.92; H, 6.78; N, 6.76%. ^{1}H NMR (CDCl$_3$): δ 1.11 (t), 1.13 (t) and 1.20 (t) (3×3H, 3Me, ^3J 7.0 Hz), 2.29 (dt, 1H, H$_A$, $^2J_{AB}$ −10.4, $^3J_{AC}$ 10.4, $^3J_{AD}$ 5.8Hz), 2.83 (dt, 1H, H$_B$, $^3J_{BC}$ 5.8, $^3J_{BD}$ 10.4 Hz) and 3.02 (ddd, 1H, H$_C$, $^2J_{CD}$ −11.6Hz), 3.08 (ddd, 1H, H$_D$), 3.43 (d, 1H, H$_F$, ^3J 12.5Hz), 4.32 (1H, H$_E$), 4.03 (m), 4.11 (m) and 4.13 (m) (3×2H, 3CH$_2$); ^{13}C NMR (CDCl$_3$): δ 13.62 (q), 13.71 (q) and 13.81 (q) (3Me, ^1J 127.9Hz), 45.36 (dd, 7-C, ^1J 138.1 and 143.9Hz), 48.22 (dd, 6-C, ^1J 138.1 and 143.9 Hz), 52.14 (dd, 3-C, ^1J 133.7, ^2J 4.4 Hz), 54.48 (dd, 4-C, ^1J 138.1, ^2J 5.8Hz), 89.81 (m) and 89.87 (m) (2-C and 4-C, ^2J, ^3J 4.4Hz), 168.14 (m) and 169.54 (m) (CO, ^2J 7.3, ^3J 4.4 Hz), 171.36 (m) and 172.1 (m) (C=O, ^3J 4.4 Hz).

[§] *Crystal data for* **3a**: $C_{13}H_{14}N_2O_7$ (from Pr^{i}OH): monoclinic, space group $P2_1/n$, at 293K: a =10.222(12), b =7.903(8), c = 18.07(2) Å, β = 102.88°, V =1423(3)Å^3, Z =4, d_{calc} =1.448 g cm^{-3}, μ = 1.19 cm^{-1}, F(000)=648. Intensities of 2760 reflections were measured with a Siemens P3/PC diffractometer at 293 K (MoKα radiation, graphite monochromator, $\theta/2\theta$-scan method, 2θ <50°), and 1480 independent observed ones with $I > 2\sigma(I)$ were used in the further calculations. The structure was solved by direct method and refined by the least-squares against F in an anisotropic-isotropic (H-atoms) approximation to R =0.065, ϖR = 0.062, GOF=1.69. All calculations were performed using the program package SHELXTL PLUS (ver. 5). Full lists of bond lengths, bond angles, atomic coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Notice to Authors, *Mendeleev Commun.*, 1997, issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 1135/13.

INTAS and the Russian Foundation for Basic Research (grants nos. 94-2839 and 94-03-08730, respectively).

References

1 R. G. Kostyanovsky, V. P. Leshchinskaya, R. K. Alekperov, G. K. Kadorkina, L. L. Shustova, Yu. I. El'natanov, G. L. Gromova, A. E. Aliev and I. I. Chervin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1988, 2566 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 2315) and references cited therein.

2 H. Bestian, *Ann.*, 1950, **566**, 210.

3 I. J. Cantlon, W. Cocker and T. B. H. McMurry, *Tetrahedron*, 1961, **15**, 46.

4 Y. Hata and M. Watanabe, *Tetrahedron Lett.*, 1972, 3827, 4659.

Received: Moscow, 14th October 1996
Cambridge, 20th November 1996; Com. 6/07096E