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Regio- and stereoselective cycloaddition of stable azomethine imines to (arylmethylidene)malononitriles

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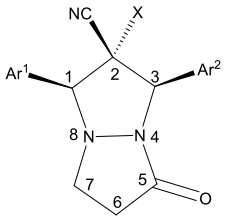
Experimental

Elemental analysis was performed by the CHN Analyzer Perkin–Elmer 2400. HRMS were measured on an MicrOTOF II (Bruker Daltonics) of the method ESI. The NMR spectra of all compounds were recorded using a Bruker AM-300 spectrometer at 300 MHz for ^{1}H and 7.47 MHz for ^{13}C spectra as well as Bruker AV-600 instrument with the frequencies 600.13 and 150.90 for ^{1}H and ^{13}C respectively, in $CDCl_3$ or DMSO-d_6. The chemical shifts of the signals of $CDCl_3$ residual proton (7.27 ppm) and carbon (77.0 ppm) as well as DMSO-d_6 (^{1}H NMR 2.50 ppm and ^{13}C NMR 39.52 ppm) were used as the internal standard. The spectra were measured at 30 °C. Aluminum TLC plates with silica gel QF 254 (Merck) were used for analytical thin-layer chromatography. Azomethine imines **9a,b** were prepared according to a reported procedures.[1] Glycine-catalyzed Knoevenagel condensation[2] of aromatic aldehydes with malononitrile and ethyl cyanoacetate gave corresponding ylidene malononitriles **3a-e**. New compounds were purified by column chromatography on silica gel, 0.060–0.200 mm, 60 A (ACROS) with AcOEt – petroleum ether as eluent. For the successful isolation of some products, silica gel was deactivated with triethylamine.[3] Quantum-chemical calculations using the Gaussian 98 program package[4] were performed at the Computing Center of Zelinsky Institute of Organic Chemistry RAS. Geometry optimizations were computed on the basis of the hybrid density functional B3LYP and standard 6-31G(d) basis set. The position of stationary points was determined using the Hessian matrix analysis by absence of imaginary frequencies for minima (and one imaginary frequency for transition state).



*(1*S**,3*R**)-1-(4-Methoxyphenyl)-5-oxo-3-phenyltetrahydropyrazolo[1,2-*a*]pyrazole-2,2(1*H*)-dicarbonitrile* **5c**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.61 – 7.35 (m, 7H, Ph, Ar), 7.00 (d, 2H, Ar, *J* 8.4 Hz), 5.71 (s, 1H, 3-H), 4.19 (s, 1H, 1-H), 3.94 – 3.69 (m, 4H, OMe, 7a-H), 3.31 – 3.11 (m, 1H, 7b-H), 2.92 – 2.72 (m, 2H, 6-H). Found: C, 70.43; H, 5.01; N, 15.72. Calculated for $C_{21}H_{18}N_4O_2$ (%): C, 70.38; H, 5.06; N, 15.63.

*(1*S**,3*R**)-3-(4-Bromophenyl)-1-(4-methoxyphenyl)-5-oxotetahydropyrazolo-[1,2-*a*]pyrazole-2,2(1*H*)-dicarbonitrile* **5d.** ^{1}H NMR (300 MHz, CDCl3): 7.60, 7.38 (both d, 4H, $H_{bromophenyl}$, *J* 8.4 Hz), 7.48, 6.99 (both d, 4H, $H_{methoxyphenyl}$, *J* 8.7 Hz), 5.64 (s, 1H, 3-H), 4.20 (s, 1H, 1-H), 3.93 – 3.69 (m, 4H, OMe, 7a-H), 3.28 – 3.13 (m, 1H, 7b-H), 2.88 – 2.72 (m, 2H, 6-H). ^{13}C NMR (75 MHz, CDCl3, δ, м.д.): 176.35 (5-C), 161.51, 158.35, 133.12, 132.44, 129.42, 128.19, 120.50, 114.84 (4-Br$\underline{C}_6H_4$, 4-MeO$\underline{C}_6H_4$), 112.86, 110.18 (2 CN), 77.15 (1-C), 65.39 (3-C), 55.34 (OMe), 44.51 (7-C), 29.09 (6-C). HRMS (ESI): calc. for $C_{21}H_{15}Br_3N_4O_2$ $[M + H]^+$: 435.0451, found 435.0453. Found: C, 57.60; H, 4.02; Br, 18.30; N, 12.76. Calculated for $C_{21}H_{15}Br_3N_4O_2$ (%): C, 57.68; H, 3.92; Br, 18.27; N, 12.81.

*(1*S**,3*R**)-1-(4-Methoxyphenyl)-5-oxo-3-(4-trifluoromethylphenyl)tetahydropyrazolo[1,2-*a*]pyrazole-2,2(1*H*)-dicarbonitrile* **5e.** ^{1}H NMR (300 MHz, $CDCl_3$): 7.75, 7.65 (both d, 4H, $H_{trifluoromethylphenyl}$, *J* 8.1 Hz), 7.50, 7.01 (оба d, 4H, $H_{methoxyphenyl}$, *J* 8.6 Hz), 5.75 (s, 1H, 3-H), 4.22 (s, 1H, 1-H), 3.94 – 3.74 (m, 4H, OMe, 7a-H), 3.34 – 3.18 (m, 1H, 7b-H), 2.83 (dd, 7.3, 2H, 6-H, *J* 9.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, м.д.): 176.70 (5-C), 161.73, 138.07, 133.92, 129.57, 127.22, 126.44, 120.45, 115.02 (4-$CF_3\underline{C}_6H_4$, 4-MeO$\underline{C}_6H_4$), 112.87, 110.17 (2 CN), 77.51 (1-C), 65.51 (3-C), 55.47 (OMe), 44.61 (7-C), 29.10 (6-C). HRMS (ESI): calc. for $C_{22}H_{17}F_3N_4O_2$ $[M - H]^+$: 425.1220, found 425.1203. Found: C, 62.03; H, 3.95; F, 13.42; N, 13.08. Calculated for $C_{22}H_{17}F_3N_4O_2$ (%): C, 61.97; H, 4.02; F, 13.37; N, 13.14.

*(1*S**,3*R**)-1-(4-Dimethylaminophenyl)-3-(4-nitrophenyl)-5-oxotetrahydropyrazolo[1,2-*a*]pyrazole-2,2(1*H*)-dicarbonitrile* **5f.** ^{1}H NMR (300 MHz, $CDCl_3$): 8.31 (d, 2H, nitrophenyl, *J* 8.6 Hz), 7.69 (d, 2H, nitrophenyl, *J* 8.6 Hz), 7.30 (d, 2H, dimethylaminophenyl, *J* 8.8 Hz), 6.67

(d, 2H, dimethylaminophenyl, *J* 8.8 Hz), 5.76 (s, 1H, 3-H), 4.27 (s, 1H, 1-H), 4.88-4.66 (m, 1H, 7a-H), 3.32 – 3.26 (m, 1H, 7b-H), 2.96 (s, 3H, NMe_2), 2.86 – 2.79 (m, 2H, 6-H). ^{13}C NMR (75 MHz, $CDCl_3$): 177.31 (5-C), 151.43, 148.11, 143.22, 129.33, 128.01, 124.05, 117.05, 112.04 (2 Ar), 113.91, 110.23 (2 CN), 77.61 (1-C), 64.42 (3-C), 63.90 (2-C), 44.87 (7-C), 40.17 (NMe_2), 29.74 (6-C). HRMS (ESI): calc. for $C_{22}H_{20}N_6O_3$ $[M - H]^+$: 416.1638, found 416.1634. Found: C, 63.53; H, 4.88; N, 20.11. Calculated for $C_{22}H_{20}N_6O_3$ (%): C, 63.45; H, 4.84; N, 20.18.

*(1*S*,2*S*,3*R*)-Ethyl 2-cyano-1-(4-dimethylaminophenyl)-3-(4-nitrophenyl)-5-oxohexahydro-pyrazolo[1,2-*a*]pyrazole-2-carboxylate* **5g.** ^1H NMR (300 MHz, CDCl3): 8.26 (d, 2H, nitrophenyl, *J* 8.7 Hz), 7.61 (d, 2H, nitrophenyl, *J* 8.7 Hz), 7.31 (d, 2H, dimethylaminophenyl, *J* 8.6 Hz), 6.70 (d, 2H, dimethylaminophenyl, *J* 8.6 Hz), 5.76 (s, 1H, 3-H), 4.34 (q, 2H, OCH_2, *J* 7.1 Hz), 4.24 (s, 1H, 1-H), 3.70 (dd, 1H, 7a-H, *J* 21.5, 9.3 Hz), 3.24 – 3.10 (m, 1H, 7b-H), 2.96 (s, 6H, NMe_2), 2.85 – 2.74 (m, 2H, 6-H), 1.30 (t, 3H, Me, *J* 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 175.99 (5-C), 165.25 ($\underline{C}O_2Et$), 151.43, 148.11, 143.22, 129.33, 128.01, 124.05, 117.05, 112.04 (2 Ar), 113.91 (CN), 76.72 (1-C), 64.30 (OCH_2), 63.84(3-C), 63.29 (2-C), 44.77 (7-C), 40.16 (NMe_2), 29.62 (6-C), 14.00 ($\underline{Me}CH_2$). HRMS (ESI): calc. for $C_{24}H_{25}N_5O_5$ $[M - H]^+$: 462.1772, found 462.1769. Found: C, 62.25; H, 5.37; N, 15.19. Calculated for $C_{24}H_{25}N_5O_5$ (5): C, 62.19; H, 5.44; N, 15.11.

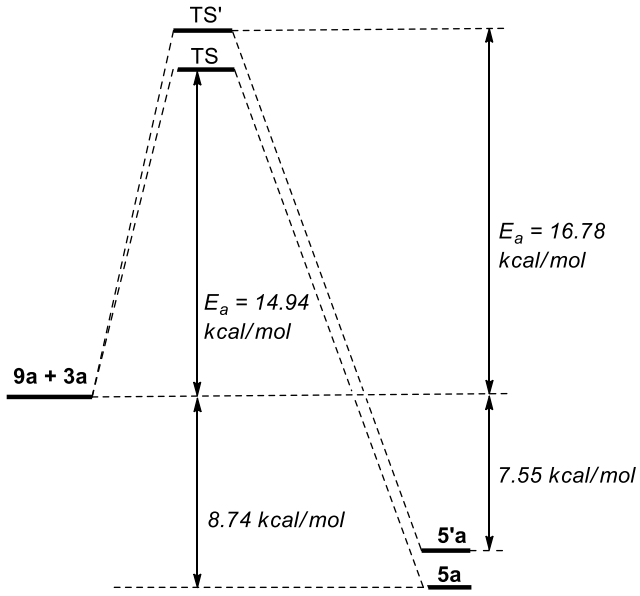


Figure 1S Energy diagram for the two plausible reaction pathways.

References

1. M Keller, A. S. Souna Sido, P. Pale and J. Sommer, *Chem. Eur. J.*, 2009, **15**, 2810.
2. J. B. Bastus, *Tetrahedron Lett*., 1963, **4**, 955.
3. (*a*) J. A. Marshall and C. A. Sehon, *Organic Syntheses*, Wiley, New York, 2004, collect. vol. 10, p. 599; (*b*) J. A. Marshall and C. A. Sehon, *Org. Synth.*, 1999, **76**, 263.
4. M. J. Frish, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr. R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, S. Clifford, J. Ochterski, G. A. Petersson, P.Y. Ayala, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, G. Liu, A. Liashenko, P. Piskorz, I. Komazomi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzales, M. Head-Gordon, E. S. Replogle and J. A. Pople, *GAUSSIAN 98, Revision A.9*, Gaussian, Inc., Pittsburgh (PA), 1998.