

PYRROLE RING OPENING IN 5-NITROSO- AND 5-PHENYLAZO-1H-PYRROLOTETRAZOLES — AN UNEXPECTED VALENCE ISOMERISM[#]

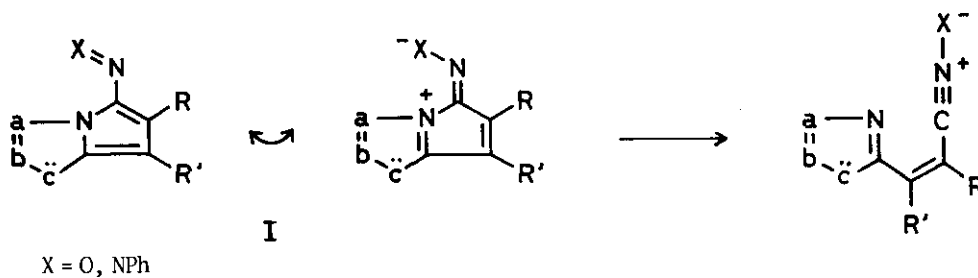
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Abstract — 1,6-Disubstituted 5-nitroso-1H-pyrrolotetrazoles ring open below 20 °C to give the isomeric acrylonitrile oxides. The 5-phenylazo analogs as well as 5-nitroso derivatives having in addition an acceptor group at C-7 are stable at 20 °C, but heating with the dipolarophile DMAD leads to pyrazoles and isoxazoles.

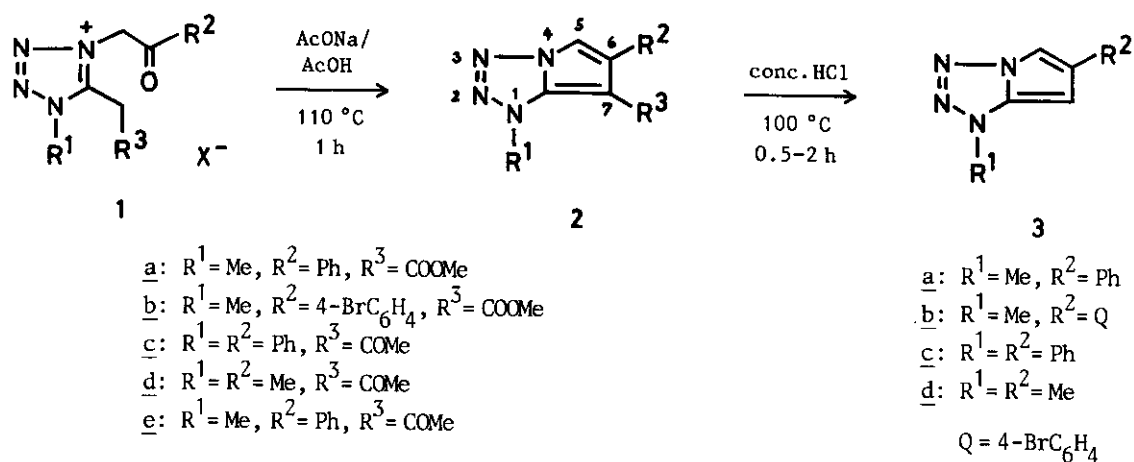
We wish to report a new valence isomerism as generalized by Scheme 1. The process shown — comparable to the nitrile-forming ring opening of five-membered heteroarenes having a nitrene function in a position α to ring oxygen, sulfur or pyrrole-like nitrogen¹ — has been encountered unexpectedly during a study on the electrophilic substitution of 1H-pyrrolotetrazoles such as **3**:

Scheme 1

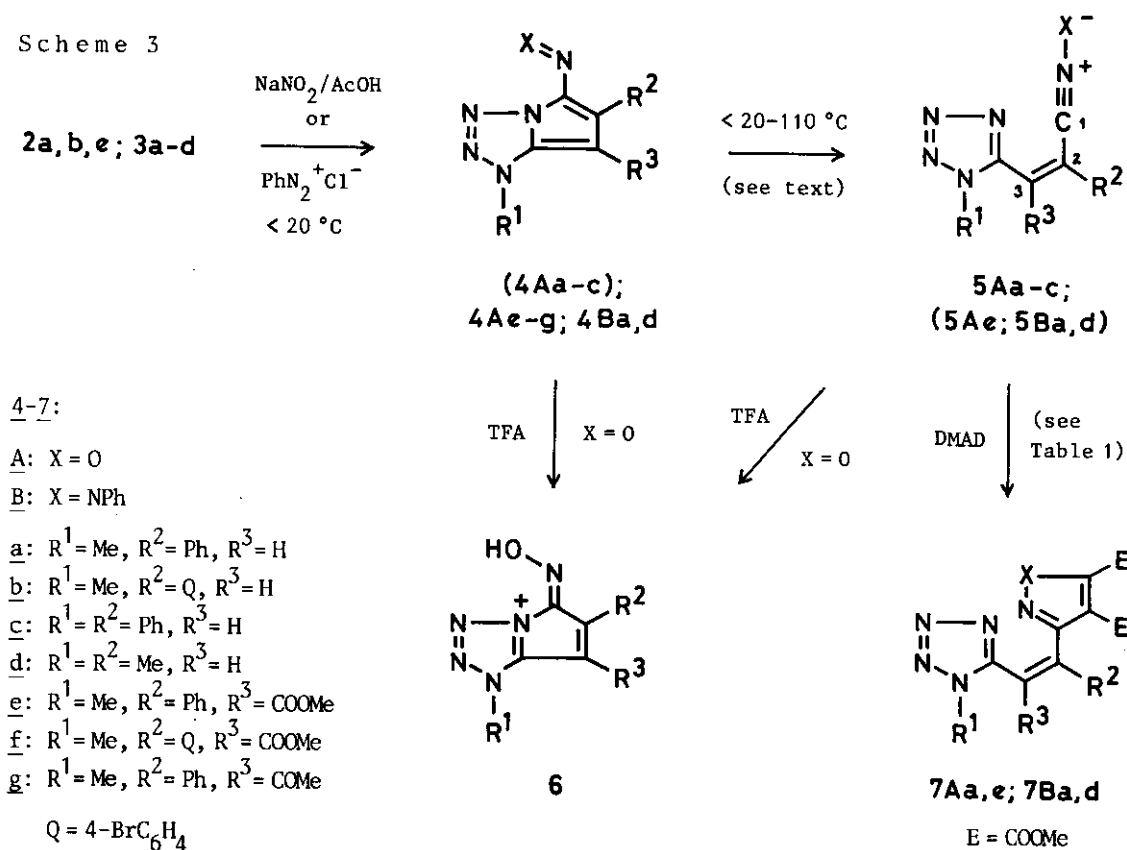


[#] Dedicated to Professor A.R.Katritzky on the occasion of his 65th birthday.

Scheme 2



Scheme 3



When the derivatives (3a-c) — novel aromatic azapentalenes, made according to Scheme 2² — were submitted to nitrosation, we isolated products that, instead of the anticipated³ nitroso compounds (4Aa-c), turned out to be the (stable) nitrile oxides (5Aa-c).⁴ The evidence is as follows (given for 5Aa): In the ir spectrum (KBr) strong absorptions at 2295 and 1385 cm⁻¹ occurred; the ¹³C nmr spectrum (DMSO-d₆) of 5Aa having a ¹⁵N-labeled CNO moiety showed a high-field shifted doublet at δ 34.7, with a coupling constant $^1J_{^{13}\text{C}, ^{15}\text{N}} = 81.0$ Hz. These data, including a ¹⁵N resonance at δ -171.0 [relative to external MeNO₂ / Cr(acac)₃], are diagnostic for a nitrile oxide function.⁵ The Z configuration of the olefinic chain formed follows from $^3J_{\text{C-1}, \text{3-H}} = 17.5$ Hz. Chemical characterization of 5Aa consists in (i) deoxygenation with triethyl phosphite to give the corresponding acrylonitrile,⁶ and (ii) [3+2] cycloaddition with DMAD to afford the isoxazole (7Aa). Recyclization of the linear isomers (5A) is feasible with strong acids, e.g. TFA. The species formed are the cations (6). This is inferred from the uv spectra which fully match those of the below mentioned isolable nitroso compounds taken in the same acidic solvent (for a comparison, see note⁷).

While the nitroso compounds (4Aa-c) isomerize spontaneously even at 0 °C, analogs that bear an electron-withdrawing substituent at C-7 such as 4Ae-g are stable under ordinary conditions. Yet, at elevated temperatures they were found to react smoothly with DMAD. For example, heating of 4Ae with the alkyne at 110 °C gave rise to the isoxazole (7Ae), an intermediate (5Ae) remaining undetected.

Quite different from the elusive nitroso derivatives (4Aa-c), 7-unsubstituted azo compounds such as 4Ba,d (prepared from 3a,d) are isolable materials. None the less, we suspected ring opening under forcing conditions. Indeed, upon prolonged heating these compounds with DMAD at 110 °C, fair yields of the pyrazoles (7Ba,d) were obtained. Again, an electron-withdrawing group at C-7 reduces the propensity for pyrrole ring cleavage appreciably; but here,

Table 1. Experimental Data of Compounds (2-5) and (7) ^{a,b}

compound	yield (%)	mp (°C)	recrystallized from	compound	yield (%)	mp (°C)	recrystallized from
<u>2a</u>	82	128-129	CHCl ₃ / Et ₂ O	<u>4Ag</u> ^f	71	141-143 ^e	CHCl ₃ / Et ₂ O
<u>2b</u>	64	114-116	CHCl ₃ / Et ₂ O	<u>4Ba</u> ^g	81	168-170 ^e	CHCl ₃ / Et ₂ O
<u>2c</u>	30	95-96	CHCl ₃ / Q ^c	<u>4Bd</u> ^g	71	128-131	CHCl ₃ / Et ₂ O
<u>2d</u>	80	152-154	CHCl ₃ / Et ₂ O	<u>4Be</u> ^g	63	240-242 ^e	CHCl ₃ / Et ₂ O
<u>2e</u>	56	92-94	CH ₂ Cl ₂ / Q ^c	<u>5Aa</u>	49	138-139 ^e	MeOH / Et ₂ O
<u>3a</u>	71 ^d	140-142	CHCl ₃	<u>5Ab</u>	34	154-155 ^e	MeOH / Et ₂ O
<u>3b</u>	58	201-203 ^e	DMF / H ₂ O	<u>5Ac</u>	67	144-146 ^e	MeOH
<u>3c</u>	70	127-129	CHCl ₃	<u>7Aa</u>	92 ^h	161-162	MeOH
<u>3d</u>	66	oil		<u>7Ae</u>	46 ⁱ	129-131	CHCl ₃ / Et ₂ O
<u>4Ae</u> ^f	78	138-140	CHCl ₃	<u>7Ba</u>	76 ^k	174-176	CHCl ₃ / Et ₂ O
<u>4Af</u> ^f	62	128-130 ^e	CHCl ₃ / Et ₂ O	<u>7Bd</u>	36 ^k	139-141	CHCl ₃ / Et ₂ O

^a Data of 1 will appear in the full paper on 1H-pyrrolotetrazoles (D.Moderhack and D.Decker, in preparation). ^b Satisfactory analytical figures (C,H,N) were obtained for all compounds listed. ^c Q = light petroleum. ^d From 2a. ^e Decont. ^f Green solid. ^g Yellow to orange solid. ^h From 5Aa / DMAD; MeOH, 65 °C; 0.5 h. ⁱ From 4Ae / DMAD; toluene, 110 °C; 2 h. ^k From 4Ba or 4Bd / DMAD; toluene, 110 °C; 24 h.

because of the lower reactivity of the 4B series in general, no reaction was observed in the case of 4Be / DMAD (as opposed to 4Ae).

Finally, we attempted ring opening of the 1H-pyrrolo[2,1-c]-s-triazole analog of 4Aa, i.e. I where a = CH, b = N, c = NMe, R = Ph, R' = H, X = O (Scheme 1). When this compound, which in contrast to 4Aa is an isolable nitroso derivative,⁸ was heated with DMAD at 110 °C for 6 h, a mere 9% yield of the 7Aa-analogous isoxazole⁹ resulted besides much tar. This shows, beyond note,³ that outside the 1H-pyrrolotetrazole series the title process seems very little favored.

Table 2. Spectral Data of Selected Compounds (2-5) and (7)

compd	ir (ν , cm^{-1} ; KBr) // ^1H / ^{13}C nmr (δ , ppm; CDCl_3 or $^*\text{DMSO}-d_6$) ^a
<u>2a</u>	3140, 1705 // 3.69 (s, 3H), 4.40 (s, 3H), 7.17 (s, 1H), 7.25-7.50 (m, 5H) / 36.7 (q), 50.6 (q), 83.6 (s), 102.6 (d), 127.6 (d), 127.7 (d, 2C), 129.7 (d, 2C), 134.1 (s), 135.7 (s), 136.2 (s), 164.0 (s)
<u>3a</u>	3140 // 3.97 (s, 3H), 5.78 (d, $J=1.4$ Hz, 1H), 7.22-7.27 (m, 1H), 7.35-7.38 (m, 2H), 7.46 (d, $J=1.4$ Hz, 1H), 7.56-7.58 (m, 2H) / 34.5 (q), 71.2 (d), 97.6 (d), 126.0 (d, 2C), 126.9 (d), 128.8 (d, 2C), 133.5 (s), 134.5 (s), 135.5 (s)
<u>4Ae</u>	1725 // 3.78 (s, 3H), 4.52 (s, 3H), 7.45-7.55 (m, 3H), 7.79-7.81 (m, 2H) / 37.6 (q), 51.8 (q), 91.5 (s), 127.5 (d, 2C), 129.9 (d), 130.0 (s), 131.8 (d, 2C), 137.0 (s), 148.6 (s), 150.4 (s), 162.4 (s)
<u>4Ba</u>	— // 4.02 (s, 3H), 6.01 (s, 1H), 7.25-7.45 (m, 6H), 7.85-7.95 (m, 4H) / 34.5 (q), 77.9 (d), 122.0 (d, 2C), 128.1 (s), 128.2 (d), 128.4 (d), 128.5 (d, 2C), 128.9 (d, 2C), 129.7 (d, 2C), 133.9 (s), 136.0 (s), 139.4 (s), 154.2 (s)
<u>5Aa</u>	2295, 1385 // * 4.22 (s, 3H), 7.54-7.57 (m, 3H), 7.86-7.88 (m, 2H), 7.89 (s, 1H) / 33.9 (q), 118.3 (d), 120.4 (s), 126.8 (d, 2C), 129.2 (d, 2C), 130.7 (d), 133.8 (s), 150.7 (s) ^b
<u>7Aa</u>	1755, 1715 // * 3.56 (s, 3H), 4.00 (s, 3H), 4.19 (s, 3H), 7.47-7.52 (m, 3H), 7.55-7.59 (m, 2H), 7.62 (s, 1H) / 33.8 (q), 52.6 (q), 53.8 (q), 113.1 (d), 115.9 (s), 127.1 (d, 2C), 128.9 (d, 2C), 130.0 (d), 136.0 (s), 136.5 (s), 150.8 (s), 156.3 (s), 159.4 (s), 160.4 (s), 160.5 (s)
<u>7Ba</u>	1745, 1720 // **3.51 (s, 3H), 3.83 (s, 3H), 3.99 (s, 3H), 6.92 (s, 1H), 7.38-7.43 (m, 8H), 7.47-7.49 (m, 2H) / 33.6 (q), 51.6 (q), 53.5 (q), 111.5 (d), 114.0 (s), 123.5 (d, 2C), 127.1 (d, 2C), 128.6 (d, 2C), 129.2 (d), 129.3 (d), 129.6 (d, 2C), 136.9 (s), 138.0 (s), 138.3 (s), 141.1 (s), 149.6 (s), 151.4 (s), 160.5 (s), 161.0 (s)

^a TMS as internal standard. ^b Signal of CNO group not observed (cf. ref.^{5b}).

REFERENCES AND NOTES

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- Cf. D.Moderhack and D.Decker, 14th International Congress of Heterocyclic Chemistry, Antwerpen, 1993, Abstracts of Papers, PO 3-211. — The direct approach from 1 where

$R^3=H$ (Chichibabin method) is vitiated by tetrazole breakdown: D.Moderhack and A.Lembcke, *Chem.Ztg.*, 1985, 109, 432.

3. Nitroso compounds of this type have been isolated, for example, in the series of pyrrolo[2,1-*b*]thiazole (a,b), 1H-pyrrolo[1,2-*a*]imidazole (c), and both 1H-pyrrolo[1,2-*b*]-(d) and 1H-pyrrolo[2,1-*c*]-*s*-triazole (e): (a) V.K.Kibirev and F.S.Babichev, *Ukr.Khim.Zh.*, 1964, 30, 488; T.Pyl and K.-H.Wünsch, *Z.Chem.*, 1965, 5, 361; (b) S.McKenzie, B.B.Molloy, and D.H.Reid, *J.Chem.Soc.C*, 1966, 1908; J.M.Tedder, K.H.Todd, and W.K.Gibson, *ibid.*, 1969, 1279; (c) A.A.Druzhinina, P.M.Kochergin, and L.M.Alekseeva, *Khim.Geterotsikl.Soedin.*, 1972, 405; (d) F.S.Babichev and V.A.Kovtunencko, *Ukr.Khim.Zh.*, 1975, 41, 181; (e) this work (see later).
4. From the reaction mixture with 3d, no definite material could be isolated.
5. (a) C.Grundmann and P.Grünanger, 'The Nitrile Oxides,' Springer-Verlag, Berlin, 1971; (b) M.Christl, J.P.Warren, B.L.Hawkins, and J.D.Roberts, *J.Am.Chem.Soc.*, 1973, 95, 4392.
6. mp 225-228 °C ($CHCl_3/Et_2O$); ir (KBr): 2230 cm^{-1} ; $^1H / ^{13}C$ nmr (DMSO- d_6): δ 4.24 (s, 3H), 7.56-7.63 (m, 3H), 7.91-7.95 (m, 2H), 8.04 (s, 1H) / 34.1 (q), 115.7 (s), 119.0 (s), 121.2 (d), 126.9 (d, 2C), 129.4 (d, 2C), 131.0 (d), 132.3 (s), 150.1 (s).
7. 6a / 6e (TFA): λ_{max} (log ϵ): 258 (4.132) / 262 (3.992), 295 (3.858) / 310 (3.939), 401 (3.850) / 415 nm (3.818) [cf. 5Aa (MeOH): 232 (3.964), 308 nm (4.247)]. — For *O*-protonation of 4A, cf. ref. 3a,d
8. Green solid, mp 203-210 °C (decompt.; DMF); ir (KBr): 3130 cm^{-1} ; 1H nmr ($CDCl_3$): δ 3.99 (s, 3H), 6.40 (d, $J=0.4$ Hz, 1H), 7.46-7.49 (m, 3H), 8.14-8.17 (m, 2H), 9.16 (br s, 1H); prepared by nitrosation of 1-methyl-6-phenyl-1H-pyrrolo[2,1-*c*]-1,2,4-triazole [mp 153-157 °C ($CHCl_3$ /light petroleum)].
9. mp 126-129 °C ($CHCl_3/Et_2O$); ir (KBr): 1740, 1715 cm^{-1} ; $^1H / ^{13}C$ nmr ($CDCl_3$): δ 3.61 (s, 3H), 3.93 (s, 3H), 4.02 (s, 3H), 7.04 (s, 1H), 7.38-7.44 (m, 5H), 7.69 (s, 1H) / 35.5 (q), 52.3 (q), 53.4 (q), 115.8 (d), 116.5 (s), 127.0 (d, 2C), 128.9 (d, 2C), 129.5 (d), 135.3 (s), 137.6 (s), 150.2 (s), 150.9 (d), 156.8 (s), 160.0 (s), 160.5 (s), 161.1 (s).

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