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

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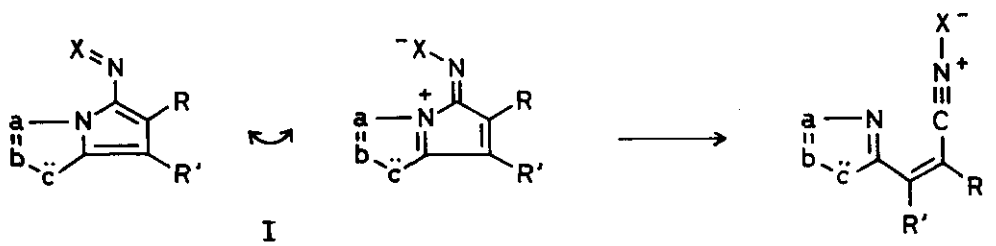
Abstract — 1,6-Disubstituted 5-nitroso-1H-pyrrolotetrazoles ring open below 20 °C to give the isomeric acrylonitrile oxides. The 5-phenylazo analogs as well as 5-nitroso derivatives having in addition an acceptor group at C-7 are stable at 20 °C, but heating with the dipolarophile DMAD leads to pyrazoles 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 nitrogen [1] — has been encountered unexpectedly during a study on the electrophilic substitution of 1H-pyrrolotetrazoles such as 3:

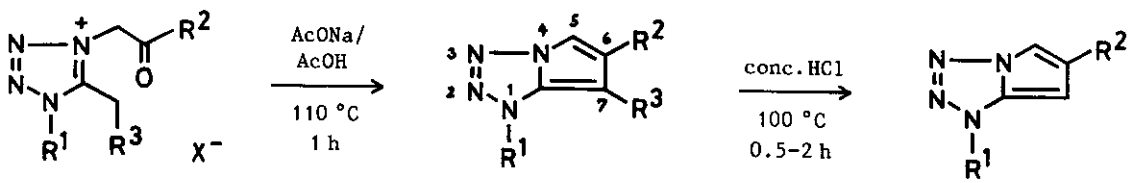
Scheme 1



X = O, NPh

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

Scheme 2



1

2

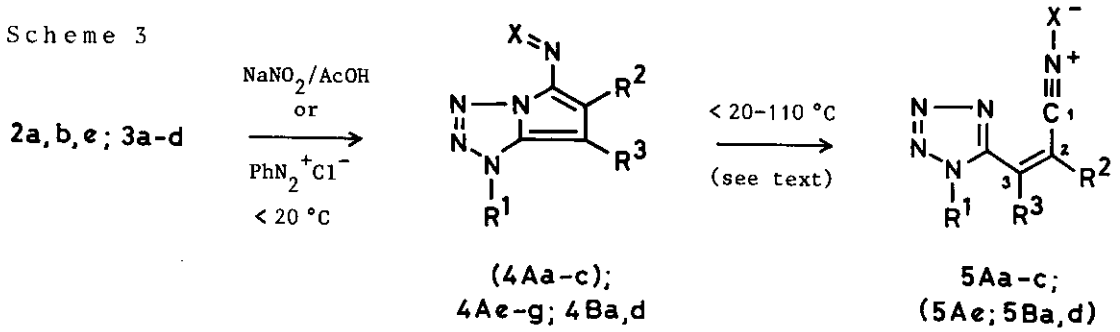
3

a: R^1 = Me, R^2 = Ph, R^3 = COOMe
b: R^1 = Me, R^2 = 4-BrC_6H_4, R^3 = COOMe
c: R^1 = R^2 = Ph, R^3 = COMe
d: R^1 = R^2 = Me, R^3 = COMe
e: R^1 = Me, R^2 = Ph, R^3 = COMe

a: R^1 = Me, R^2 = Ph
b: R^1 = Me, R^2 = Q
c: R^1 = R^2 = Ph
d: R^1 = R^2 = Me

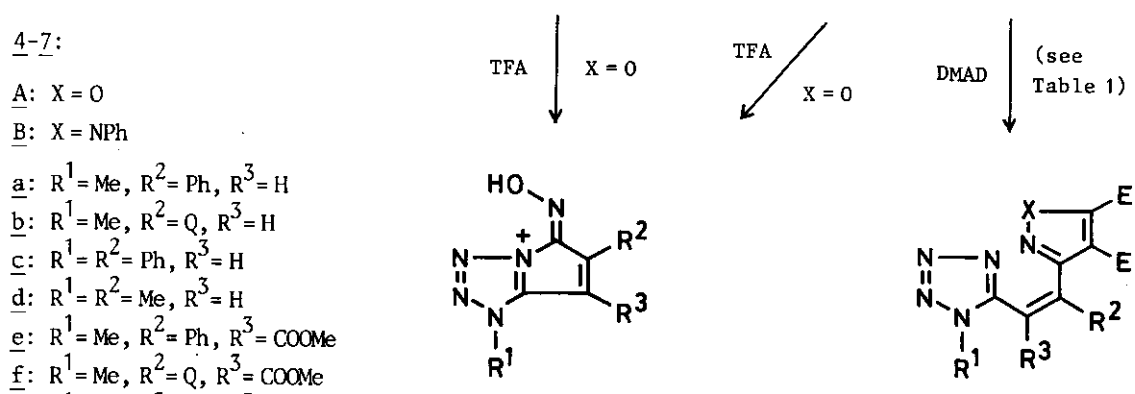
Q = 4-BrC_6H_4

Scheme 3



(4Aa-c); 4Ae-g; 4Ba,d

5Aa-c; (5Ae; 5Ba,d)



6

7Aa,e; 7Ba,d

E = COOMe

4-7:

A: X = O
B: X = NPh

a: R^1 = Me, R^2 = Ph, R^3 = H
b: R^1 = Me, R^2 = Q, R^3 = H
c: R^1 = R^2 = Ph, R^3 = H
d: R^1 = R^2 = Me, R^3 = H
e: R^1 = Me, R^2 = Ph, R^3 = COOMe
f: R^1 = Me, R^2 = Q, R^3 = COOMe
g: R^1 = Me, R^2 = Ph, R^3 = COMe

Q = 4-BrC_6H_4

When the derivatives (3a-c) — novel aromatic azapentalenes, made according to Scheme 2 [2] — were submitted to nitrosation, we isolated products that, instead of the anticipated [3] 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 ^{13}C nmr spectrum (DMSO-d_6) of 5Aa having a ^{15}N-labeled CNO moiety showed a high-field shifted doublet at δ 34.7, with a coupling constant $^{1}J_{^{13}C,\,^{15}N} = 81.0$ Hz. These data, including a ^{15}N resonance at δ -171.0 [relative to external $MeNO_2$ / $Cr(acac)_3$], are diagnostic for a nitrile oxide function.[5] The Z configuration of the olefinic chain formed follows from $^{3}J_{C\text{-}1,\,3\text{-}H} = 17.5$ 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 note [7]).

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
2a	82	128-129	$CHCl_3$ / Et_2O	4Ag [f]	71	141-143 [e]	$CHCl_3$ / Et_2O
2b	64	114-116	$CHCl_3$ / Et_2O	4Ba [g]	81	168-170 [e]	$CHCl_3$ / Et_2O
2c	30	95-96	$CHCl_3$ / Q [c]	4Bd [g]	71	128-131	$CHCl_3$ / Et_2O
2d	80	152-154	$CHCl_3$ / Et_2O	4Be [g]	63	240-242 [e]	$CHCl_3$ / Et_2O
2e	56	92-94	CH_2Cl_2 / Q [c]	5Aa	49	138-139 [e]	MeOH / Et_2O
3a	71 [d]	140-142	$CHCl_3$	5Ab	34	154-155 [e]	MeOH / Et_2O
3b	58	201-203 [e]	DMF / H_2O	5Ac	67	144-146 [e]	MeOH
3c	70	127-129	$CHCl_3$	7Aa	92 [h]	161-162	MeOH
3d	66	oil		7Ae	46 [i]	129-131	$CHCl_3$ / Et_2O
4Ae [f]	78	138-140	$CHCl_3$	7Ba	76 [k]	174-176	$CHCl_3$ / Et_2O
4Af [f]	62	128-130 [e]	$CHCl_3$ / Et_2O	7Bd	36 [k]	139-141	$CHCl_3$ / Et_2O

[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] Decompt. [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 isoxazole [9] 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 *DMSO-d_6) [a]
2a	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)
3a	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)
4Ae	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)
4Ba	— // 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)
5Aa	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]
7Aa	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)
7Ba	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

1. Overview: W.Dehaen and J.Becher, Acta Chem.Scand., 1993, 47, 244; cf. also J.A.Hickman and D.G.Wibberley, J.Chem.Soc., Perkin Trans.1, 1972, 2958.

2. 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.Kovtunenko, 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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