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INTRAMOLECULAR 2H GROUP-TRANSFER IN HETEROCYCLIC BRIDGED-RING SYSTEMS (DYOTROPIC REARRANGEMENTS[1])

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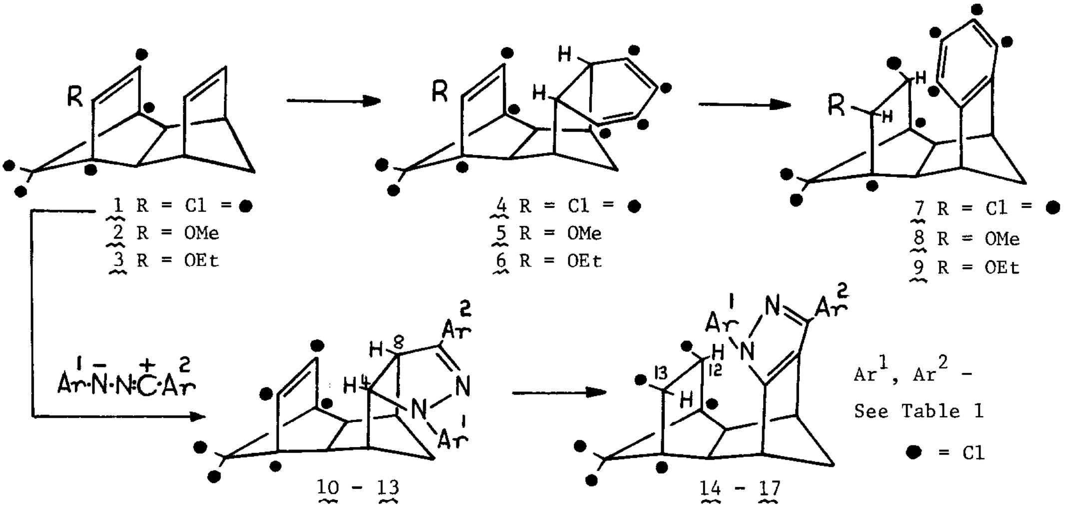
Abstract: Diarylnitrilimines, derived by thermolysis of appropriate diaryltetrazoles, form $(4+2)\pi$ cyclo-adducts with dipolarophiles of the isodrin type, e.g. (1); the resulting 2-pyrazolines thermally rearrange into pyrazoles by hydrogen group transfer. Kinetic data for examples of this and related reactions are reported.

Since the intramolecular concerted double group-transfer[2] of hydrogen atoms in a non-catalysed thermal sigmatropic rearrangement was first clearly recognised (viz: 4,5,6 → 7,8,9)[3a] there have been very few reports of other examples[4] of this theoretically interesting[2,5] and occasionally useful[6] reaction. Those examples which we have previously disclosed are all essentially irreversible exothermic reactions[3b] in which the aromatisation of the diene-ring and release of ring-strain at the receptor π-bond clearly provides substantial driving force.



Analogous but thermoneutral and reversible hydrogen transfer reactions in oxygen-bridged systems having critical stereochemical features in common with compounds 4-6 have also been reported recently, with relevant kinetic data,[7] (vide infra).

In the meantime we have investigated the synthesis and behaviour of compounds having the same framework as in structures 4-6 but with a heterocyclic ring replacing the cyclohexadiene element. In preliminary experiments[8] isodrin, 1, heated with several 3,6-diaryl-1,2,4,5-tetrazines (in CCl_4 or C_6H_5Me at the b.p.) gave products of dinitrogen extrusion from the initial inverse electronic demand $(4+2)\pi$ cyclo-adducts; these products have ^1H NMR and UV spectra characteristic of pyridazine derivatives resulting from intramolecular hydrogen transfer from the diarylated 4,5-dihydropyridazine ring in an intermediate analogous to 4.[9]

These observations prompted the question: does hydrogen transfer occur in compounds with a smaller-sized heterocyclic ring as intramolecular hydrogen donor, and if so, how readily?

2,5-Diaryl-1,2,3,4-tetrazoles[10] are convenient sources of diarylated 1,3-dipolar reagents;[11] accordingly isodrin 1, (1:1 - 2:1 mol.excess), heated with a range of diaryltetrazoles (PhBr, 157° 3-6h) and preparative TLC of the products (silica gel, 4:1 petroleum/Et_2O) gives 2-pyrazoline derivatives e.g. 10-13 (Table 1) in up to $\sim$80% yield.[12] In every case a small quantity of an isomeric higher m.p. adduct is also isolated ($\sim$6%) which lacks the intensity of visible blue fluorescence emission at 450-465 nm strikingly characteristic of most of the pyrazoline derivatives made. Heating each of the pyrazolines 10-13 (157°, $\sim$48h, N_2) gives the respective pyrazole isomer 14-17 (Table 1) identical to the minor products noted above. The nature of the isomerisation as a double hydrogen group transfer is most clearly reflected in the 2-pyrazoline and pyrazole ^{1}H NMR spectra; each type exhibits two doublets (H-4,8 and H-12,13) in the range 3.4-4.4δ but whilst for the pyrazolines these signals are broadened by further coupling, in the isomeric pyrazoles the pairs of doublets diverge and each is exceptionally sharp, consistent with the relevant nuclei being in a non-protonated environment. Characteristic differences are also seen in the electronic (UV) spectra for the isomer-pairs, the pyrazolines having medium wavelength λ_{max} at 340-360 nm (ε 1.5-2.2 x 10^4) shifted to 280-299 nm (ε 2.0-2.6 x 10^4) in the pyrazoles, (Table 1). Systematic changes also appear in the IR C=N stretching region (1400-1600 cm^{-1})[13] the most notable being the shift of a strong band near 1400 cm^{-1} in the pyrazolines to $\sim$1460 cm^{-1} in the pyrazoles.

Qualitatively, all the pyrazolines rearrange at comparable rates (e.g. k_1(10):k_1(12) is $\sim$1.5 at 196°); Beers Law holding at the appropriate concentration (3.6 x 10^{-5} M) UV absorption facilitates kinetic measurements and heating pyrazoline 10 (degassed decalin solutions, sealed *in vacuo*[14]) over the range 185-205° gives good first order rate plots and the data in Table 2, from which Eyring parameters (Table 4) are computed.[15] The data may be compared to those similarly obtained (decalin solutions in air) for the pentacyclic trienes 4 and 6[16] (Tables 3,4), e.g. compounds 6 and 9 not being affected by oxidising agents.[3b]

Table 1

Pyrazolines							Pyrazoles				
	Ar^1	Ar^2	M.p.[a]	H-4,8[b]	λ_{max}[c]	Emiss.[c]		m.p.	H-12,13[d]	λ_{max}[c]	Emiss.[c]
10	Ph	Ph	220°	4.37,3.91	358	452	14	277-9°	3.62,4.47	280,285,291	335
11	p-MeC_6H_4	p-MeC_6H_4	230°	4.35,3.88	360	462	15	257-8°	3.61,4.49	283,288,295	343
12	p-ClC_6H_4	p-ClC_6H_4	251°	4.36,3.89	366	465	16	266-8°	3.46,4.32	286[e],291,299	342
13	p-MeC_6H_4	p-ClC_6H_4	229°	4.39,3.87	371	454	17	258-9°	3.61,4.42	288,297[e]	346

[a] ±1°; some samples resolidify as pure pyrazole

[b] All ^{1}H NMR δ values refer to $CDCl_3$/TMS solution each signal dm, ^3J $\sim$10 Hz

[c] UV λ_{max} and fluorescence emission in nm for ethanol solution

[d] Each signal sharp doublet ^3J 9-11Hz

[e] Shoulder

Order of fluorescence intensities ($\sim 10^{-6}$M): 12 >> 10 $\sim$ 13 >> 11 and 16 >> 17 > 14 $\sim$ 15.

Table 2

Unimolecular Rate Constants for Rearrangement of 2-Pyrazoline, **10**

Temp. (^{o}C):	185.7^{o}	190.1^{o}	196.0^{o}	201.3^{o}	205.2^{o}
k_1, s^{-1} x 10^5:	3.35	4.77	7.35	10.8	14.0

Table 3

Unimolecular Rate Constants for Rearrangement of Trienes **4** and **6**

4:	Temp. (^{o}C):	79.8^{o}	82.2^{o}	84.8^{o}	87.7^{o}	90.0^{o}	95.0^{o}	96.0^{o}
	k_1, s^{-1} x 10^5:	3.85	4.85	6.26	8.46	10.6	16.6	18.4
6:	Temp. (^{o}C):	99.8^{o}	105.0^{o}	107.0^{o}	109.8^{o}	115.0^{o}	115.2^{o}	120.0^{o}
	k_1, s^{-1} x 10^5:	1.68	2.87	3.46	4.59	7.32	7.72	11.3

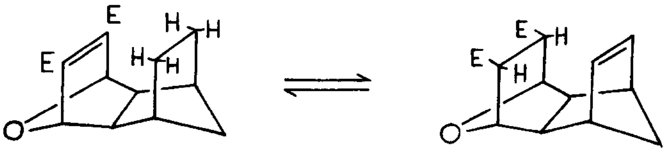
Table 4

Eyring Activation Parameters for Rearrangement of **4**, **6** and **10**

	ΔE_a $^{(a)}$	$\Delta H^{\ddagger(a)}$	$\Delta S^{\ddagger(b)}$	$\Delta G^{\ddagger(a)}$	log A
4	25.07 ± 0.17	24.48 ± 0.17	-9.76 ± 0.09	27.39	11.09 ± 0.10
6*	27.69 ± 0.35	27.08 ± 0.35	-8.22 ± 0.14	29.53	11.43 ± 0.20
10	32.00 ± 0.31	31.41 ± 0.30	-11.30 ± 0.15	34.78	10.76 ± 0.14

$^{(a)}$kcals mol^{-1}; $^{(b)}$cal mol^{-1}K^{-1}; *Similar data apply to compound **5**; k_1(**5**): k_1(**6**) is 1.17 at 120^{o}.

Vogel *et al.*[7] in their kinetic study of a thermally neutral intramolecular hydrogen transfer, with transannular π-switching not concerted with aromatisation, (**18** $\rightleftharpoons$ **19**) found a small positive $\Delta S^{\ddagger}$ value. In the examples discussed here the appreciably negative $\Delta S^{\ddagger}$ term probably reflects concomitant transition state stiffening as the aromatic rings develop. Comparison of the data for compounds **10** and **4** is consistent with pyrazoline aromatisation providing less driving force, but increased strain associated with rehybridisation of the heterocyclic ring must also be a contributory factor. Although differences in aryl substitution in the pyrazolines appear to have only a relatively small effect, substituent changes at the primary reaction site have a notable influence (*cf.* **4** and **6**);[16] and this is also dramatically seen in the diphenylnitrilimine adducts of dechloroethoxy compound, **3**, which are little changed after heating 100h (157^{o})! (*cf.* ref. 9).



18 (E = CO_2Me)

19

$\Delta H^{\ddagger}$ = 35 - 39 kcal mol^{-1}

$\Delta S^{\ddagger}$ = 2 - 11 cal mol^{-1}K^{-1}

(**18** $\longrightarrow$ **19**)

1. *Cf*. M.T. Reetz, *Tetrahedron* (1973), *29*, 2189; *Angew Chem. I.E*. (1972), *11*, 129, 130.

2. R.B. Woodward and R. Hoffmann "*The Conservation of Orbital Symmetry*", Verlag Chemie (1970), p. 141.

3. (a) K. Mackenzie, *J.Chem.Soc*. (1965), 4646; (b) *ibid*, p.4650; (c) K. Mackenzie, *J.Chem.Soc.C* (1969), 1784. K. Mackenzie and C.H.M. Adams, *ibid* (1969), 480.

4. *Cf*. R. Srinivasan, *Tetrahedron Letters* (1973), 4029. D. Ginsburg describes intramolecular dehydrogenation of an ethano bridge by a neighbouring azo function: *Tetrahedron*, (1974), *30*, 1487; cf. S. Hünig, H.R. Müller and W. Thier, *Angew Chem.I.E*. (1965), *4*, 271.

5. *Cf*. D.F. Feller, M.W. Schmidt and K. Ruedenberg, *J.Amer.Chem.Soc*., (1982), *104*, 960.

6. K.B. Astin, A.V. Fletcher, K. Mackenzie, A.S. Miller, K.W. Muir, A.A. Frew and N.M. Ratcliffe, *J.Chem.Soc.Perkin II*, (1982), 111. H. Prinzbach, G. Sedelmeier, C. Krüger, R. Goddard, H.-D. Martin and R. Gleiter, *Angew Chem.I.E*., (1978), *17*, 271.

7. J.-P. Hagenbuch, B. Stampfli and P. Vogel, *J.Amer.Chem.Soc*., (1981), *103*, 3934. In this connexion, thermolysis of dihydro- **1** shewed no evidence of group transfer to the ClC=CCl element (K. Mackenzie and D.L. Williams-Smith, unpublished work).

8. J. Franklin, K. Mackenzie and M.L. Kitchen, unpublished work, (see ref. 12).

9. However a similar reaction with dechloroethoxy compound **3** and 3,6-di(2'-pyridyl)tetrazine gave a dihydropyridazine derivative[8] (^{1}H NMR and UV absorption) which shewed little if any group transfer rearrangement at $\sim$160°.

10. S. Ito, Y. Tanaka, A. Kakehi, K. Kondo, *Bull.Chem.Soc. Japan*, (1976), *49*, 1920.

11. R. Huisgen, M. Seidel, G. Wallbillich and H. Knupfer, *Tetrahedron*, (1962), *17*, 3.

12. All new compounds characterised by elemental composition and mass spectrometry, in addition to ^{1}H NMR, IR, UV and fluorescence emission spectra, as appropriate.

13. C.J. Ponchert "*Aldrich Library of I.R. Spectra*" (third edition) (1981), Aldrich Chemical Co. Inc.

14. In one instance, heating compound **10** in air gave an oxide derivative and attempted kinetic measurements in air shewed non first-order behaviour.

15. We thank Dr. J.P. Maher and Herr G. Mrotzek for facilities and a computer programme. Data are for 25°C.

16. These compounds were prepared as previously described[3a] and purified by preparative TLC; decomposition of the bridge-carbonyl precursor of triene **4** was *ca*. 75% complete after 2½h in boiling *dilute* CCl$_4$ solution. Original samples of triene **4** had completely rearranged after *ca*. 18 years at room temperature, but compounds **5** and **6** remained unchanged during this time.

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