

Competing Pathways in the Phototransposition of Pyrazoles

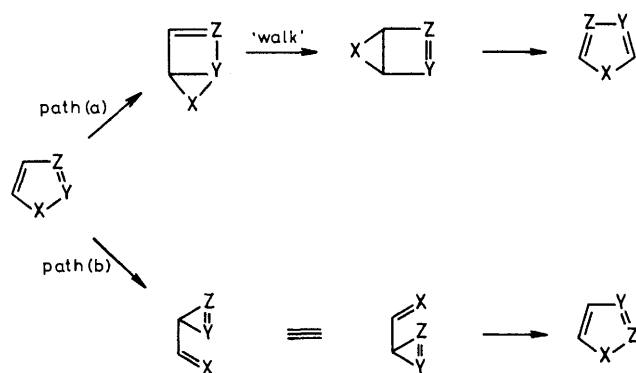
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Summary Cyano-substituted pyrazoles transpose photochemically into imidazoles by two concurrent paths: (a) 1,5-interchange, probably by 2,5-bonding to a diazabicyclopentene which isomerises by nitrogen 'walk'

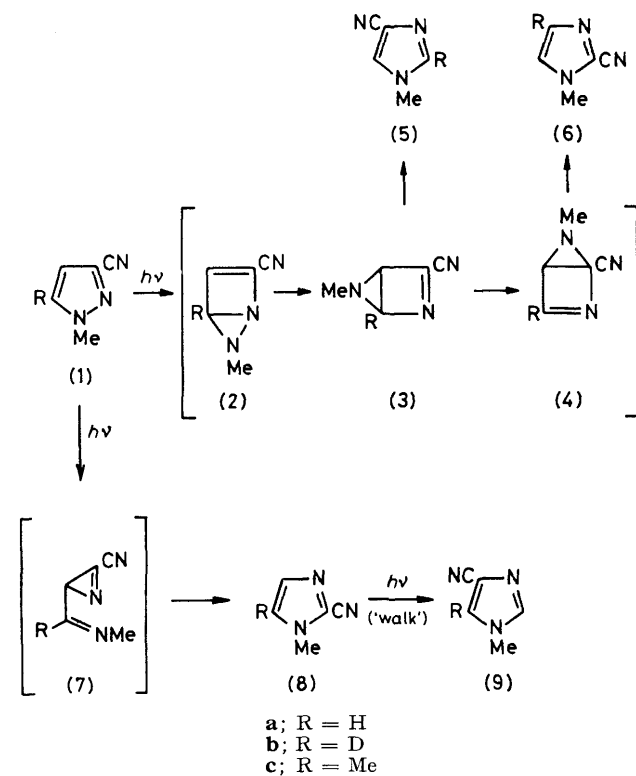
before rearomatisation, and (b) 2,3-interchange, probably *via* an intermediate azirine; in sharp contrast, 1,5-dimethyl-3-trifluoromethylpyrazole phototransposes exclusively by the former path.

PHOTOTRANSPOSITIONS of 5-membered heteroaromatic compounds are mechanistically complex and varied,¹ but two general types of mechanism can be discerned: (a) 2,5-bonding followed by 'walk' of the heteroatom in an intermediate heterocyclic bicyclopentene [path (a) in Scheme 1;



SCHEME 1

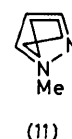
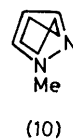
e.g. imidazoles,² X = NR, Y = CR', Z = N]; and (b) 2,3-interchange *via* a ring-contracted 3-vinylcyclopropene heterologue [path (b); *e.g.* furans,³ X = O, Y = CR, Z = CR']. What determines which path a given system adopts is unclear, and, in this connection, the phototransposition of pyrazoles (X = NR; Y = N; Z = CR') into imidazoles^{2,4} has particular interest in that both paths seem to be implicated (*cf.* aryl-substituted oxazoles⁵); the



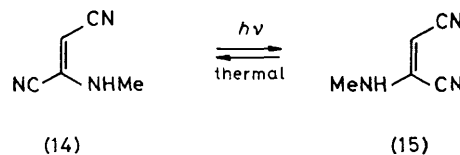
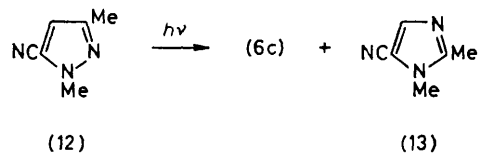
SCHEME 2

system therefore offering an opportunity of exploring the competing factors upon which paths (a) and (b) depend. Accordingly, and considering the effect of a CN substituent in the photochemistry of thiophens⁶ and pyrroles,⁷ we have studied the effects of introducing the groups CN and CF₃ upon pyrazole photochemistry.

Irradiation† of 3-cyano-1-methylpyrazole (**1a**) in acetonitrile gave 2-cyano-1-methylimidazole (**8a**) (25%) and 4-cyano-1-methylimidazole (**5a**) (11%). Discrimination between the two hydrogen-bearing ring atoms C(4) and C(5) was achieved by irradiation of the 5-deuterio-analogue (**1b**) (80–85% D), which gave compounds (**8b**) and (**5b**), thereby establishing the permutation patterns^{7,8} as, respectively, (**10**) and (**11**). Thus, the imidazole (**8a**) very probably arises *via* path b [(**1**) → (**7**) → (**8**)] and the imidazole (**5a**) *via* path a [(**1**) → (**2**) → (**3**) → (**5**)], the path (a): path (b) ratio being 0.44:1. Sensitisation and quenching experiments indicated that the reactive excited state of the pyrazole (**1**) (and of all the other pyrazoles studied here) had the singlet π, π^* configuration.

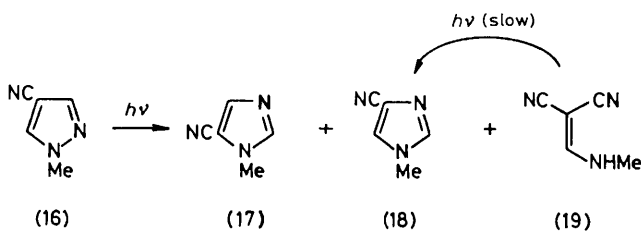


Irradiation† of 3-cyano-1,5-dimethylpyrazole (**1c**) gave, in addition to the analogous products (**5c**) (5.5%) and (**8c**) (16%), the isomeric imidazoles (**6c**) (3.5%) and (**9c**) (4%). The possibility that the imidazole (**6c**) arose by secondary irradiation of compound (**5c**) by the imidazole 'walk' mechanism² [(**5**) → (**3**) → (**4**) → (**6**)] was excluded by an independent irradiation of (**5c**), which gave no (**6c**), which suggests that (**6c**) arises directly from excited (**1c**) by a double 'walk' process [(**1**) → (**2**) → (**3**) → (**4**) → (**6**)]. This double 'walk' has analogy in the photochemistry of cyanothiophens⁶ and 5-methyl-substituted 2-cyanopyrroles.⁷ Independent irradiation of the path b product (**8c**) gave the imidazole (**9c**), and so, in the irradiation of (**1c**), (**9c**) is probably a secondary photoproduct. However, the possibility that the product (**9c**) also arises, in part, directly from the pyrazole (**1c**) by some totally new process has not yet been rigorously excluded. If (**9c**) is assumed to arise solely *via* (**8c**), the path (a): path (b) ratio [(**5**) + (**6**): (**8**) + (**9**)] in the transposition of (**1c**) is 0.45:1.



† Reactants were irradiated as 0.002–0.02M solutions in acetonitrile degassed with nitrogen, with a 100W medium-pressure mercury arc lamp. Quoted yields are yields isolated by preparative layer chromatography after destruction of >90% of the starting material.

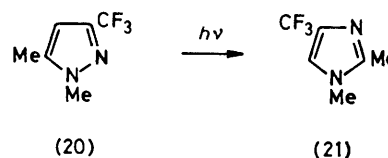
5-Cyano-1,3-dimethylpyrazole (**12**) transposed similarly, albeit less efficiently (10% combined yield),[†] to give 2-cyano-1,4-dimethylimidazole (**6c**) and 5-cyano-1,2-dimethylimidazole (**13**). The corresponding permutation patterns, (**11**) and (**10**) respectively, suggest that (**6c**) arises by path (a) with single 'walk' of the NMe group, and (**13**) by path (b). The path (a):path (b) ratio was *ca.* 1:1. 5-Cyano-1-methylpyrazole gave analogous products and, in addition, 2-methylaminofumaronitrile (**14**). The formation of this cleavage product, which has various precedents,^{4,9-12} probably involves the migration, in some acyclic species which occurs in path (b), of the hydrogen atom originally situated at C(3). Photochemically, the fumaronitrile isomerised to the corresponding maleonitrile (**15**) and showed no evidence of cyclisation with skeletal rearrangement to an imidazole, unlike certain related β -aminoacrylonitriles.¹³ [Contrast this with the case of isomer (**19**), below.] The maleonitrile (**15**) slowly reverted in solution to (**14**) in the dark.



Irradiation[†] of 4-cyano-1-methylpyrazole (**16**) gave the imidazoles (**17**) and (**18**), and methylaminomethylene-malononitrile (**19**) in respective yields of 10, 25, and 45%. The malononitrile (**19**) underwent photochemical conversion into the 4-cyanoimidazole (**18**) (*cf.* ref. 13), but far too slowly to account for more than a small fraction of the imidazole (**18**) produced in the irradiation of (**16**). Consequently, most of this product must arise from (**16**) more directly, presumably by ring-expansion of a path (b) azirine analogous to compound (**7**). The 5-cyanoimidazole (**17**) is very probably a path (a) photoproduct of (**16**). Ring-atoms C(4) and C(5) were discriminated by irradiation of 5-deuterated (**16**), which yielded 2-D-(**17**) and 5-D-(**18**), thus confirming that (**17**) and (**18**) are formed by permutation patterns, (**11**) and (**10**), respectively, consistent with the respective derivations of these imidazoles from the path (a) and path (b) re-

arrangements of (**16**). Hence, on the assumption that the malononitrile (**19**) is a path (b) by-product [*cf.* (**14**) from 5-cyano-1-methylpyrazole, above], the path (a):path (b) ratio in this system is 0.14:1.

Evidently, path (b) competes somewhat more efficiently with path (a) in this 4-cyanopyrazole than in the 3- and 5-cyanopyrazoles. However, the chief point in the present context is that, contrary to the case of pyrroles⁷ and thiophenes,⁶ a CN substituent introduces no gross, qualitative effect upon pyrazole photochemistry. Thus, the less ambiguous[‡] of the reported^{2,4} phototranspositions of simple methyl-substituted pyrazoles apparently range from pure path (b) cases to one in which path (a) is dominant [1,3,5-trimethylpyrazole, path (a):path (b) ratio 2.5:1 in cyclohexane²]. The double 'walk' [(**1c**) \rightarrow (**6c**)] that we observe appears novel in pyrazole photochemistry, but such processes could be concealed in the published examples,^{2,4} which lack sufficient positional labelling.



In striking contrast, irradiation[†] of 1,5-dimethyl-3-trifluoromethylpyrazole (**20**) gave solely 1,2-dimethyl-4-trifluoromethylimidazole (**21**) (41%), the product of permutation pattern (**11**) and therefore of path (a). Similar results were obtained in ethanol and cyclohexane. This promotion by a CF_3 group of 2,5-bonding has some analogy in the photochemical valence isomerisation of tetrakis(trifluoromethyl)thiophen.¹⁴

Rationalisation of the substituent effects reported herein and elsewhere^{6,7} must await the results of MO calculations currently in hand. However, substituent-induced perturbation of the photochemistry of 5-membered heteroaromatics obviously merits further experimental study.

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[†] In no case was complete discrimination of the ring atoms achieved. In the work of Tiefenthaler *et al.* (ref. 4), most of the examples were N-H pyrazoles, where further ambiguity exists owing to the possibility of prototropic tautomerism.

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