Tetrahedron Letters No. 13, pp 1101 - 1104, 1975. Pergamon Press. Printed in Great Britain.

OXAZOLINES, THIAZOLINES, OXAZOLES, THIAZOLES AND PYRAZOLES FROM ALLENIC AND ACETYLENIC NITRILES

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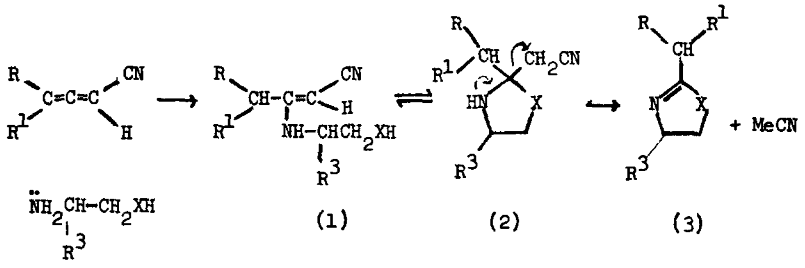
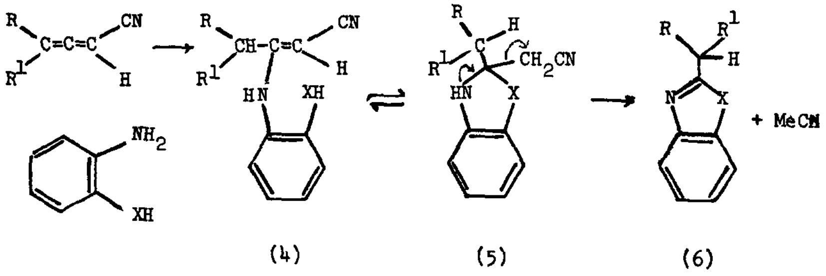
(Received in UK 27 January 1975; accepted for publication 19 February 1975)

We have recently shown [1] that double Michael addition of ethylene- and phenylene diamines to allenic and acetylenic nitriles was followed by elimination of acetonitrile to give 2-substituted imidazolines and benzimidazoles in >80% yield. In view of the ready availability of the starting materials and the synthetic and biological importance of heterocycles containing nitrogen, and either oxygen or sulphur, we have extended our investigations to these systems.

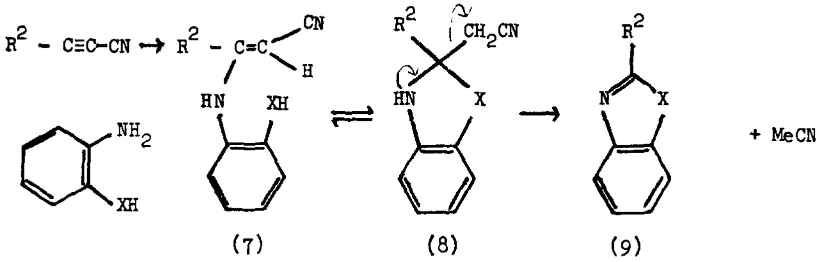
We now report the quantitative addition of equimolar amounts of ethanolamines, o-aminophenols, β-aminoethanethiols, or o-aminobenzenethiols to allenic [2] or acetylenic [3] nitriles and the cyclisation of the resulting adducts to oxazolines, oxazoles, thiazolines and thiazoles in 70-90% yield (see Table).



(1) (2) (3)



(4) (5) (6)



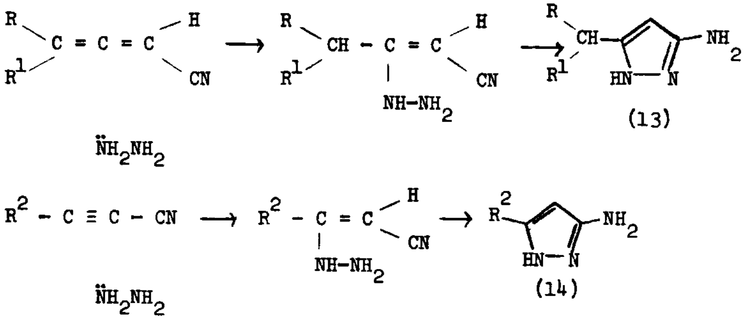
(7) (8) (9)

[X = O or S] [R^3 = H or alkyl]

The Michael adducts (1), (4) and (7) [where X = O] are distilled at atmospheric pressure, when first of all acetonitrile and then the oxazoline (3) [X = O] or the benzoxazole (6) or (9) [X = O] are collected.

The adducts (1), (4) and (7) [where X = S] do not cyclise spontaneously on heating but have to be treated with catalytic quantities of a base, e.g. sodium ethoxide. Distillation at atmospheric pressure gave acetonitrile followed by the thiazolines (3) [X = S] or the benzthiazoles (6) or (9) [X = S]. We believe that initially the oxazolidines and the thiazolidines (2), (5) and (8) [X = 0 or S] are formed and these then eliminate acetonitrile, thus displacing the equilibrium to the right. Clearly certain substituents e.g. phenyl can only be introduced in the 2-position by using the acetylenic nitrile but in most cases the allenic nitriles, which are easier to prepare, react more smoothly without the formation of biproducts.

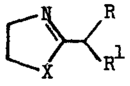
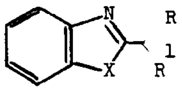
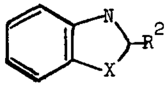
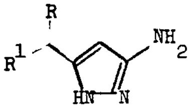
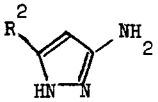
The addition of 2,3-butadienenitrile to excess hydrazine hydrate has previously been shown[4] to give 3-amino-5-methylpyrazole. We have found that on mixing equivalent quantitites of either acetylenic or allenic nitriles containing a variety of substituents with hydrazine hydrate and keeping at 100° for 30 min. a near quantitative yield of 5-substituted 3-aminopyrazoles (13) or (14) is obtained (see Table).



(13)

(14)

TABLE

	R	R^1	R^2	X = O		X = S	
				Yield(%)	m/e	Yield(%)	m/e
* 	Me	Me		76	113		
	Me	Et		72	127	65	143
	Pr	H		76	127		
* 	Me	Me				70	177
	Me	Et		81	175	82	191
	Pr	H		70	175		
* 			Ph			76	211
				Yield(%)	m/e		
* 	Me	Me		96	125		
	Me	Et		85	139		
	Me	Bu^t		80	167		
	Pr	H		96	139		
* 			Ph	95	159		

* All heterocycles had satisfactory elemental analyses and spectral properties in accord with the assigned structures.

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