

Reactions of Diene-conjugated 1,3-Dipolar Intermediates: the Formation of Cycloprop[*c*]isoquinolines from Benzonitrile *o*-Alkenylbenzyl Ylides and their Rearrangements to 2-Benzazepines

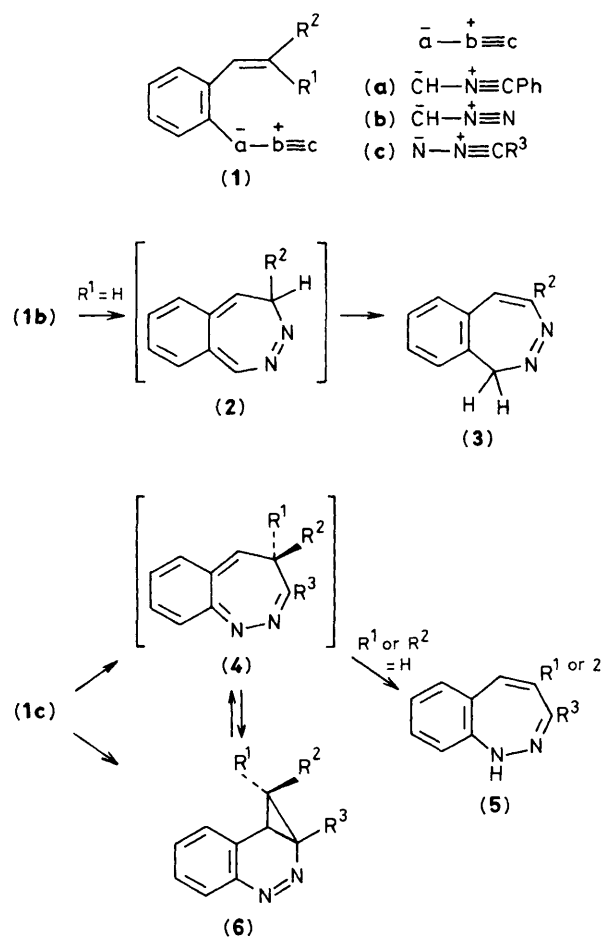
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The $\alpha,\beta:\gamma,\delta$ -unsaturated nitrile ylides (**9**), when generated by the 1,3-dehydrochlorination of the benzimidoyl chlorides (**8**) at room temperature, react by a stereospecific 1,1-cycloaddition to give the cycloprop[*c*]isoquinolines (**10**); the latter undergo two types of thermal rearrangement giving the 1*H*-2-benzazepines (**14**) when R^1 or $R^2 = H$, and the 5*H*-2-benzazepines (**17**) when $R^1 = Ph$ and $R^2 = Ph$ or Me.

This communication is concerned with the reactions of the diene-conjugated nitrile ylides (**1a**). The objective was to compare their reactions with those of the analogous diazo-compounds (**1b**) and nitrile imines (**1c**). Recent work has shown that both (**1b**) and (**1c**) cyclise to give seven-membered heterocyclic systems, (**3**) and (**5**) respectively, but *via* reaction paths which show interesting and not fully understood differences. The diazo-compounds (**1b**; $R^1 = H$) apparently cyclise directly *via* 1,7-electrocyclisation to give (**2**) which rearrange to give (**3**) by [1,5] sigmatropic hydrogen shifts.¹⁻³

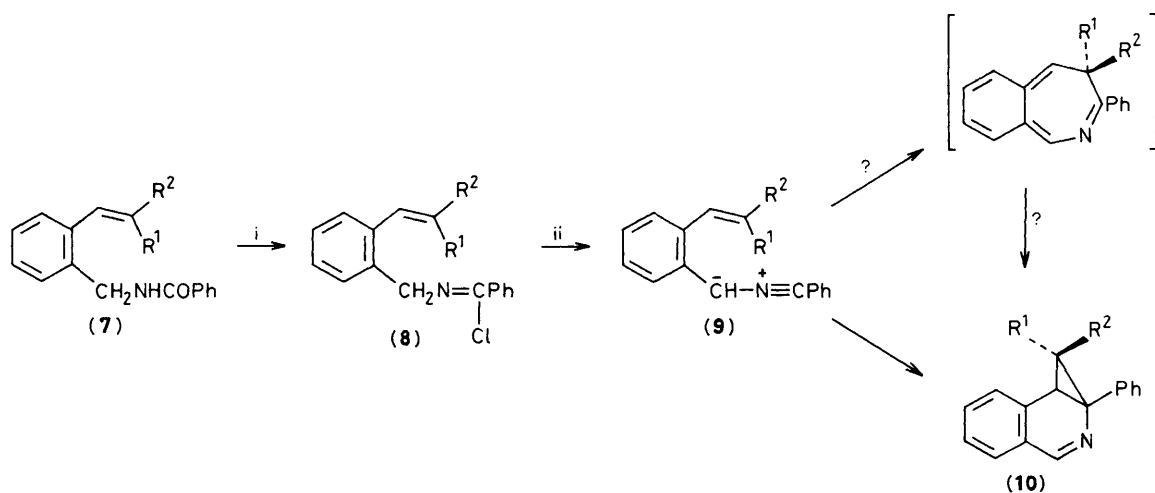
This cyclisation is however blocked when $R^1 \neq H$; *e.g.* the diazo-compounds (**1b**; $R^1 = Me$ or Ph , $R^2 = H$) react only *via* loss of nitrogen to give carbene-derived products.³ The nitrile imines (**1c**; R^1 or $R^2 = H$) undergo a formally similar conversion at 80 °C to give the 1,2-benzodiazepine system (**5**), but when neither R^1 nor $R^2 = H$ give instead the tricyclic system (**6**).^{4,5} Subsequent work however has shown that at room temperature the nitrile imines give only (**6**) in a highly stereoselective reaction, irrespective of whether R^1 or $R^2 = H$.⁶ It is not yet clear whether these cyclopropacino-



lines (6) are formed directly in a one-step stereospecific 1,1-cycloaddition process or *via* (4) in a two-step mechanism in which the ring contraction of (4) to give (6) must be much faster than its rate of ring inversion.

One example of the analogous nitrile ylide system (1a; $R^1 = R^2 = H$) has been studied by Padwa. This system was generated by the photolysis of an azirine and gave (10, $R^1 = R^2 = H$).⁷ Since nitrile ylides generated by this method have been shown to give non-stereospecific 1,1-cycloadditions in related non-conjugated systems,⁷⁻⁹ our intention was to use a non-photochemical method to generate a range of intermediates of type (9) to find out: (i) if this process is stereospecific like the nitrile imine cyclisation, (ii) if the reaction with the double bond is blocked when $R^1 \neq H$ as it is in the diazo-compound reaction, and (iii) if compounds of type (10) would undergo thermal ring expansion and so provide a synthetic route to fully unsaturated 2-benzazepine systems.

It was found that the required nitrile ylides (9a-h) could be generated by reaction of the benzimidoyl chlorides (8) with potassium *t*-butoxide at room temperature. On addition of the base an intense transient red colour was generated, and after work-up and flash chromatography the cycloprop[c]isoquinolines (10) were isolated, Scheme 1. It can be seen from these results that the reaction of the nitrile ylide with the double bond is not inhibited by the presence of R^1 groups other than hydrogen and that the 1,1-cycloaddition is stereospecific under these reaction conditions. The stereospecificity is shown clearly by the observation that the separated *E* and *Z* isomers of the amide, (7a) and (7b), gave, respectively, only the *exo* and *endo* isomers (10a) and (10b) together with some unreacted starting material. In two other cases (7c/d) and (7e/f) it was not possible to separate the *E* and *Z* isomers at any stage but it was shown by n.m.r. spectroscopy (using the nuclear Overhauser effect to identify the *E* and *Z* isomers) that the *exo/endo* ratios in (10) were, within experimental

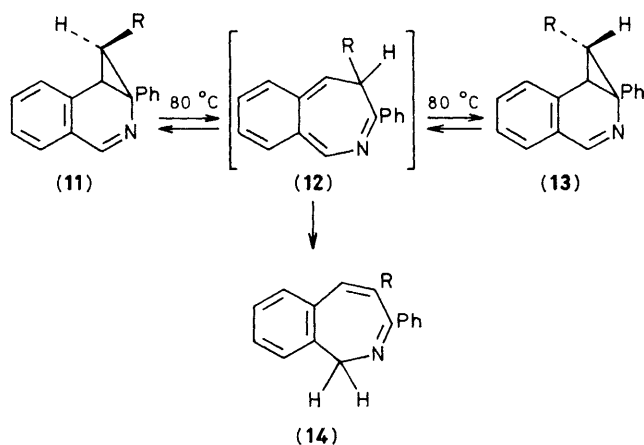


(7)		(10) (% yield)	
(a)	$R^1 = H, R^2 = Ph$	(a)	$R^1 = H, R^2 = Ph$ (85)
(b)	$R^1 = Ph, R^2 = H$	(b)	$R^1 = Ph, R^2 = H$ (73)
(c)/(d)	$R^1, R^2 = Me$ and H (<i>Z</i> : <i>E</i> = 68:32)	(c)	$R^1 = H, R^2 = Me$ (72)
(e)/(f)	$R^1, R^2 = Me$ and Ph (<i>Z</i> : <i>E</i> = 63:37)	(d)	$R^1 = Me, R^2 = H$ (56)
(g)	$R^1 = R^2 = Me$	(e)	$R^1 = Me, R^2 = Ph$ (79)
(h)	$R^1 = R^2 = Ph$	(f)	$R^1 = Ph, R^2 = Me$ (91)
		(g)	$R^1 = R^2 = Me$
		(h)	$R^1 = R^2 = Ph$

(d:c = 69:31)

(f:e = 60:40)

Scheme 1. Reagents: i, PCl_5 ; ii, $KOBu^t$ in tetrahydrofuran.



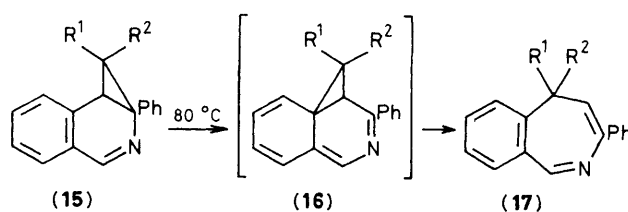
Scheme 2

	% Yield
R = Ph	70
R = Me	92

error, the same as the *E/Z* ratios of the amide mixtures used.[†] These results therefore closely parallel the reactions of the analogous nitrile imines (1c).

Investigation of the thermal rearrangement of the cycloprop[c]isoquinolines (10) has revealed two distinct reaction paths. In cases where either R¹ or R² = H heating causes the interconversion of the *endo* and *exo* isomers, (11) and (13), Scheme 2, and the eventual formation of the 1H-2-benzazepine system (14) in high yield. When neither R¹ nor R² was hydrogen the rearrangement was slower and followed an alternative path, Scheme 3, to give 5H-2-benzazepines (17). The structure of (17a) was confirmed by X-ray crystallography.¹⁰

[†] The *exo* and *endo* isomers of (10) were separated and characterised in all cases.



Scheme 3

	% Yield
(a) R ¹ , R ² = Me/Ph	51
(b) R ¹ = R ² = Ph	74

Work on the kinetics of some of these reactions is in progress and discussion of the mechanisms of the formation and rearrangement of the cycloprop[c]isoquinolines (10) will be deferred until the full paper.

We thank the University of Edinburgh and the S.E.R.C. for studentships (to I.R.R. and K.R.M.).

Received, 29th August 1984; Com. 1236

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