A Simple Route to C-Functionalised Azaxylylenes and Diazaxylylenes

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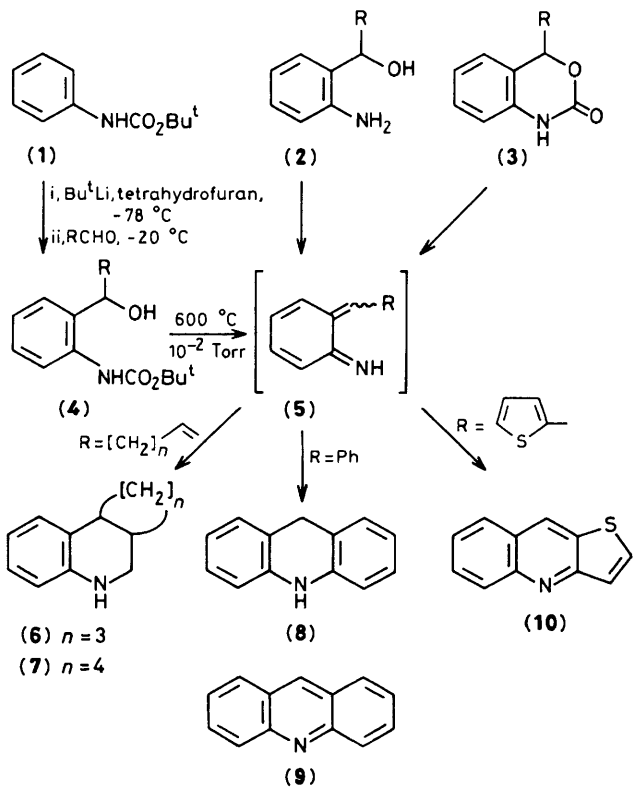
o-Lithiation of t-butoxycarbonylaniline and 4-t-butoxycarbonylaminopyridine followed by reaction with aldehydes gives t-butoxycarbonylamino alcohols which are converted into azaxylylenes and diazaxylylenes on flash pyrolysis.

Azaxylylenes (**5**) are reactive species with considerable potential in heterocyclic synthesis,[1,2] however, so far, only *N*-substituted azaxylylenes have found application.

Our reported[1] flash vacuum pyrolysis (FVP) of *o*-aminobenzyl alcohols (**2**) and dihydro-1,3-benzoxazin-2-ones (**3**) lends itself to the production of C-functionalised azaxylylenes since the amino alcohols and hence dihydrobenzoxazinones are, in principle, available by nucleophilic addition to *o*-aminophenylcarbonyl compounds. In practice, addition of Grignard or organolithium reagents to *o*-aminobenzaldehyde, *o*-nitrobenzaldehyde, or *o*-nitrobenzoic acid failed and additions to anthranilic acid, isatoic anhydride, or 1,3-benzoxazin-4-ones gave the desired products in low yields only. For example, the dihydrobenzoxazinones (**3**; R = pent-4-enyl and hex-5-enyl) were obtained in overall yields of 17 and 14% respectively by treatment of 2-methyl-1,3-benzoxazin-4-one with the alkenyl Grignard reagent followed by hydrolysis, reduction, and reaction with phosgene.

An alternative, superior approach to these amino alcohols involves addition of *o*-lithiated t-butoxycarbonylaniline (**1**) to the appropriate aldehydes.[3] Thus, the t-butoxycarbonylamino alcohols† (**4**; R = pent-4-enyl, hex-5-enyl, Ph, and 2-thienyl) were obtained in 57, 30, 50, and 14% yield respectively, in a one-pot procedure.

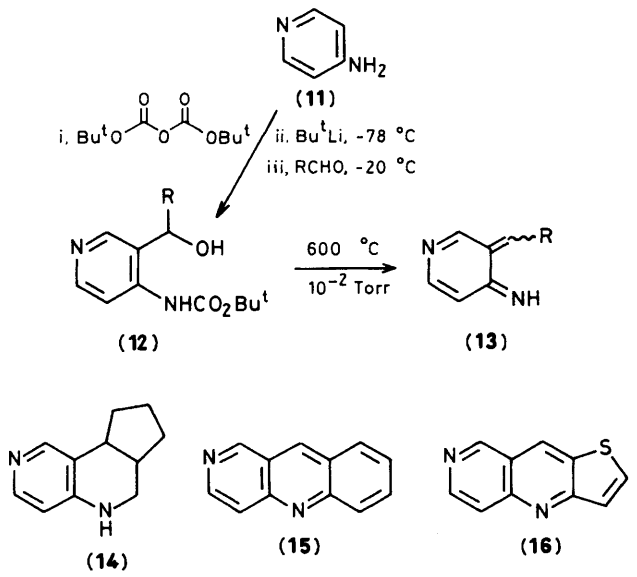
Deprotection of the amino group was found to be unnecessary and indeed FVP of the t-butoxycarbonylamines (**4**)



† All new compounds were fully characterised and had satisfactory analytical and spectral data.

directly was distinctly advantageous in that the urethanes (**4**) were more volatile than the amines (**2**) and decomposed smoothly to give the azaxylylenes at temperatures somewhat lower than the amines (550 °C *cf.* 700 °C). This decomposition may involve loss of isobutene, CO_2, and H_2O or formation of an intermediate dihydrobenzoxazin-2-one by loss of t-butyl alcohol and then extrusion of CO_2.

On FVP at 600 °C the pentenyl and hexenyl t-butoxycarbonyl derivatives (**4**; R = $[CH_2]_3CH{=}CH_2$ and $[CH_2]_4CH{=}CH_2$) gave the intramolecular Diels–Alder adducts (**6**) 21% and (**7**) 30% respectively, demonstrating for the first time that C-substituted azaxylylenes undergo this potentially very important type of reaction. In contrast the corresponding amino alcohols (**2**) gave no intramolecular Diels–Alder adducts; presumably 1,2-dehydration dominates. On the other hand the corresponding dihydrobenzoxazinones (**3**) which lead to the xylylenes by a retro Diels–Alder reaction which precludes 1,2-dehydration gave the adducts (**6**) and (**7**) cleanly and in high yield.



Adduct (**6**) was stereochemically pure with m.p. 38—41 °C identical to that reported for the tentatively assigned *cis*-isomer.[4] Adduct (**7**) had m.p. 42—44 °C also corresponding to that reported for the *cis*-isomer;[5] however, the 250 MHz ^1H n.m.r. spectrum indicated a 3 : 1 mixture of *cis* : *trans*-isomers. A *cis*-stereochemistry for these adducts is consistent with an *endo*-transition state for the intramolecular Diels–Alder reaction which must proceed with the azaxylylene in an *E*-configuration.

The t-butoxycarbonylamine (**4**; R = Ph) gave dihydroacridine (**8**) and acridine (**9**) on FVP by electrocyclisation of the azaxylylene (**5**; R = Ph). The thiophene derivative (**4**; R = 2-thienyl) gave the thienoquinoline (**10**) (54%) showing that this type of electrocyclisation is general.

The potential of this approach to azaxylylenes is underlined by the generation of the diazaxylylenes (**13**; R = pent-4-enyl, Ph, and 2-thienyl) as the first heterocyclic analogues of azaxylylenes. This was accomplished in three steps from 4-aminopyridine (**11**) by t-butoxycarbonylation, lithiation and treatment with the appropriate aldehyde, and FVP of the resulting urethanes (**12**). These diazaxylylenes gave, respectively, the intramolecular Diels–Alder adduct (**14**) m.p. 235—237 °C (64%), the naphthyridine (**15**),[6] quantitatively, and the thienonaphthyridine (**16**) (66%).

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References

1 R. D. Bowen, D. E. Davies, C. W. G. Fishwick, T. O. Glasbey, S. J. Noyce, and R. C. Storr, *Tetrahedron Lett.*, 1982, 4501.
2 Y. Ito, S. Miyata, M. Nakatsuka, and T. Saegusa, *J. Am. Chem. Soc.*, 1981, **103**, 5250; Y. Ito, E. Nakajo, M. Nakatsuka, and T. Saegusa, *Tetrahedron Lett.*, 1983, 2881.
3 J. M. Muchowski and M. C. Venati, *J. Org. Chem.*, 1980, **45**, 4798.
4 B. K. Blount, W. H. Perkin, and S. G. Preston Plant, *J. Chem. Soc.*, 1929, 1975.
5 T. Masamune, M. Takasugi, H. Suginome, and M. Yokayoma, *J. Org. Chem.*, 1964, **29**, 681.
6 A. T. Loscia and S. C. Dickerman, *J. Am. Chem. Soc.*, 1959, **81**, 3098.