Synthesis of Tetrahydro-1*H*-benzo-1,5-diazepines

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Summary Reaction of equivalent amounts each of *o*-phenylenediamine and potassium cyanide with a number of αβ-unsaturated carbonyl compounds in the presence of acetic acid (3—5 mol. equiv.) provides a convenient new synthesis of tetrahydro-1*H*-benzo-1,5-diazepines.

WE recently reported[1] that reaction of equivalent amounts of cinnamaldehyde, potassium cyanide, acetic acid, and *o*-phenylenediamine gave the *o*-aminoanilinonitrile (**1a**). We now find that when excess of (3—5 equiv.) acetic acid is used, an isomer of (**1a**), a tetrahydro-1*H*-benzo-1,5-diazepine (**2a**), is obtained in excellent yield.

TABLE

Yields and melting points of benzodiazepines (**2**)

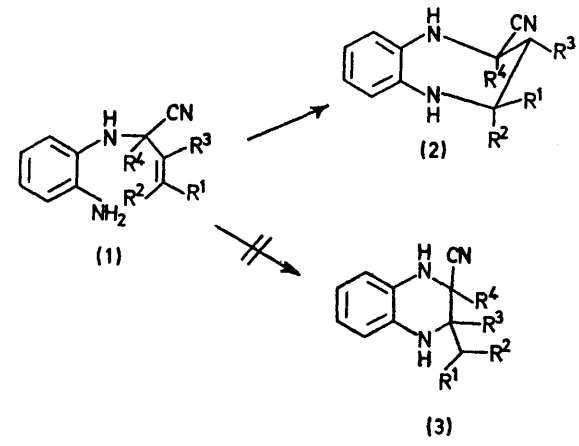
Compound[a]	R^1	R^2	R^3	R^4	Yield (%)	M.p. (°C)
a	Ph	H	H	H	99	134—135
b	Me	H	H	H	86	159—161
c	2-Furyl	H	H	H	68	122—123·5
d	2-Thienyl	H	H	H	63	155—156
e	Ph	H	H	Me	90	155—157
f	Me	H	Me	Me	74	165—168
g	Me	Me	H	Me	35	141—142·5[4]

[a] New compounds gave satisfactory analytical data.

The product was assigned structure (**2a**) on the basis of its spectral data [i.r., u.v., n.m.r., and mass spectra]. Structure (**2a**) rather than (**3a**) was confirmed by its 100 MHz n.m.r. spectrum at 80°. The n.m.r. spectrum of (**2b**) gave unequivocal evidence for structure (**2**) rather than (**3**) since the methyl protons gave a doublet [δ 1·33 p.p.m. (*J* 6 Hz)].

Several benzodiazepines (**2**) have been prepared in good yields from various αβ-unsaturated carbonyl compounds (see Table). The apparent generality of this method is important since the reaction of *o*-phenylenediamine with a number of αβ-unsaturated carbonyl compounds is reported[3] to give a Schiff base, a benzimidazole, or a benzodiazepine depending on the structure of the carbonyl compound.

Under the usual conditions for the synthesis of α-aminonitriles,[2] only (**1a**) and (**1c**) were obtained, while (**1b**), and



(**1d**)—(**1g**) could not be isolated; instead here only the cyclized products (**2b**), and (**2d**)—(**2g**), were formed respectively. It appears that the α-aminonitrile (**1**) is a likely intermediate in the formation of (**2**) since refluxing of a solution of (**1a**) in ethanol for 2 h gave benzodiazepine (**2a**) in good yield.

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