

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

By JASJIT SINGH WALIA,\* LINDA A. HEINDL, AMRIK SINGH WALIA, and PARVEEN S. WALIA

[Department of Chemistry, Loyola University (New Orleans), New Orleans, Louisiana 70118]

**Summary** Reaction of equivalent amounts each of *o*-phenylenediamine and potassium cyanide with a number of  $\alpha\beta$ -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<sup>1</sup> that reaction of equivalent amounts of cinnamaldehyde, potassium cyanide, acetic acid, and *o*-phenylenediamine gave the *o*-aminoanilinnitrile (**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 <sup>a</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	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 <sup>4</sup>

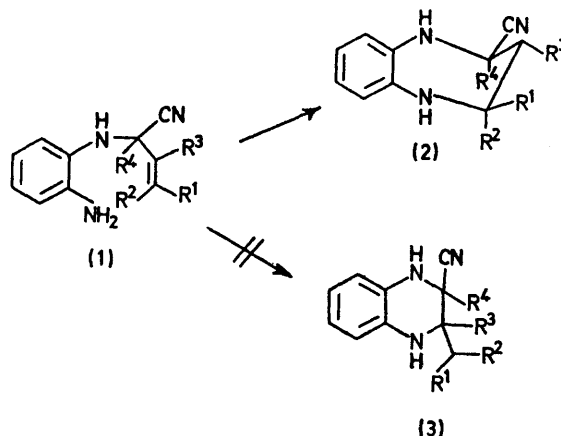
<sup>a</sup> New compounds gave satisfactory analytical data.

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 [ $\delta$  1.33 p.p.m. ( $J$  6 Hz)].

Several benzodiazepines (**2**) have been prepared in good yields from various  $\alpha\beta$ -unsaturated carbonyl compounds (see Table). The apparent generality of this method is

important since the reaction of *o*-phenylenediamine with a number of  $\alpha\beta$ -unsaturated carbonyl compounds is reported<sup>3</sup> 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  $\alpha$ -aminonitriles,<sup>2</sup> 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  $\alpha$ -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.

Financial support from the Edward G. Schlieder Educational Foundation and Hoffman-LaRoche, Inc., is acknowledged.

(Received, 25th May 1972; Com. 898.)

<sup>1</sup> J. S. Walia, P. S. Walia, L. A. Heindl, and P. Zbylot, *J.C.S. Chem. Comm.*, 1972, 108.

<sup>2</sup> J. S. Walia, P. S. Walia, H. Lader, and L. Heindl, *Chem. Comm.*, 1967, 1290.

<sup>3</sup> W. Reid and P. Stahlhofen, *Chem. Ber.*, 1957, **90**, 815.

<sup>4</sup> Lit. m.p. 144°, S. Bodforss, *Annalen*, 1971, **745**, 99.