Synthesis and Photochemical Behaviour of 3*H*-1,2-Benzodiazepines

By JYOJI KURITA and TAKASHI TSUCHIYA*

(*School of Pharmaceutical Sciences, Showa University, Shinagawa, Tokyo, Japan*)

Summary The previously unknown 3*H*-1,2-benzodiazepines (**3**) are prepared from the 1*H*-isomers (**1**) in high yields and the energy barriers to ring inversion are estimated from n.m.r. spectral data; irradiation of the diazepines (**3**) affords 3-vinylindazole and indenes.

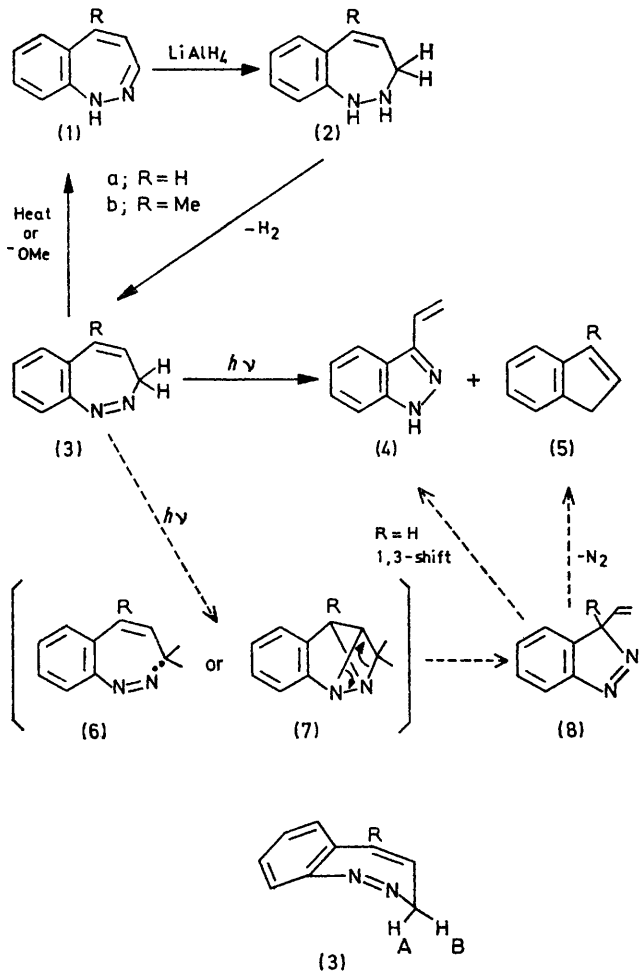
RECENTLY we reported[1] the synthesis of 1*H*-1,2-benzodiazepines (**1**) and we were interested in the preparation of the tautomeric 3*H*- and 5*H*-1,2-benzodiazepines, in connection with studies on 1,2-diazepines[2,3] and 2,3-benzodiazepines.[4] We report here the synthesis of the 3*H*-1,2-benzodiazepines (**3**) and some of their thermal and photochemical reactions.

The benzodiazepines (**2**), prepared by $LiAlH_4$ reduction of the benzodiazepines (**1**), were dehydrogenated with 4-phenyl-1,2,4-triazoline-3,5-dione in dry benzene to give compounds (**3**) quantitatively:† (**3a**) b.p. 125—128° at 1 mmHg; δ (CS_2 at 34°) 4·00br (2H, d, 3-H), 5·75 (1H, m, 4-H), 6·72 (1H, d, 5-H), and 7·2—7·8 (4H, m, Ar-H); (**3b**) b.p. 132—134° at 1 mmHg, δ (CS_2 at 34°) 2·12br (3H, 5-Me), 2·2—5·5br (2H, 3-H), 5·62 (1H, m, 4-H), and 7·2—7·7 (4H, m, Ar-H). The 3*H*-diazepines (**3**) were readily tautomerized to the parent 1*H*-diazepines (**1**) by treatment with NaOMe in MeOH or heating in CCl_4 at 150° in a sealed tube.

Irradiation (400 W high-pressure Hg lamp; Pyrex) of the diazepine (**3a**) in CH_2Cl_2 solution gave 3-vinylindazole (**4**; 90%)‡ and indene (**5a**; 1—2%). Under similar conditions, 5-methyldiazepine (**3b**) gave 3-methylindene (**5b**; *ca.* 70%) but no indazole derivative. This result indicates that the formation of (**4**) and (**5**) may involve proton transfer and

† Satisfactory elemental analyses and mass spectral data were obtained for all new compounds and the indenes (**5**) were identified by comparison with the authentic samples.

‡ Compound (**4**): m.p. 117·5—118·5°, δ ($CDCl_3$) 5·52 (1H, dd, *J* 11 and 1·5 Hz), 6·07 (1H, dd, *J* 16 and 1·5 Hz), 7·06 (1H, dd, *J* 11 and 16 Hz), 7·0—7·9 (4H, m, Ar-H), and 11·0br (1H, NH).



extrusion of nitrogen of the key intermediates (**8**), which are formed *via* the diradical (**6**) or the tetracyclic intermediates (**7**), and not tautomerization to the 1*H*- or 5*H*-isomers followed by ($_{\pi}2_s$ + $_{\pi}2_s$) reaction of the azabutadiene units to the tricyclic compounds analogous to that observed for 2,3-benzodiazepines.[4]

The n.m.r. spectrum of the 3*H*-benzodiazepines (**3**) showed a similar temperature dependence to those of 4*H*-1,2-diazepines,[2] and 1*H*- and 5*H*-2,3-benzodiazepines[4] consistent with the predictable temperature-dependent inversion of the diazepine ring. The C-3 methylene protons of (**3a**) show a doublet at δ 4·00 (**3b**: 3·98) at 100°, which broadens with decreasing temperature and splits into ABX quartets centred on δ 2·20 and 5·80 (**3b**: 2·22 and 5·67) below the coalescence temperature, the change being complete at −80°; the rest of the spectrum is essentially unchanged. The energies of activation for ring inversion were calculated by spectral analysis (see Table).

TABLE. N.m.r. spectral parameters for C-3 methylene groups in compounds (**3**) at 90 MHz.[a]

Compound	$\Delta\nu_{AB}$[b]/Hz (±1)	J_{AB}/Hz (±0·5)	T_c[c]/°C (±5)	$\Delta G^{\ddagger}$/kcal mol^{-1} at T_c[d]
(**3a**)	324·0	12	−20	11·7±0·3
(**3b**)	310·5	12	25	13·8±0·3

[a] Spectra were measured on a Hitachi R-22 Spectrometer in CS_2. [b] Chemical shift difference at −80° in Hz. [c] Temperature of coalescence. [d] The free energies of activation for ring inversion ($\Delta G^{\ddagger}$) were calculated using the formula: $k_c = \pi(\Delta\nu_{AB}^2 + 6J_{AB}^2)^{\frac{1}{2}}/\sqrt{2}$ (ref. 5).

The energy barriers to ring inversion are lower than those recorded for the monomeric diazepines and 2,3-benzodiazepines. The $\Delta G^{\ddagger}$ value for (**3b**) increases most probaby because of increased steric interaction in the transition state between 5-Me and the *peri*-hydrogen on the aromatic ring.

(*Received, 4th September* 1974; *Com.* 1134.)

[1] T. Tsuchiya, J. Kurita, H. Igeta, and V. Snieckus, *J.C.S. Chem. Comm.*, 1974, 640.
[2] O. Buchardt, C. L. Pedersen, U. Svanholm, A. M. Duffield, and A. T. Balaban, *Acta Chem. Scand.*, 1969, **23**, 3125.
[3] A. J. Carty, R. F. Hobson, H. A. Patel, and V. Snieckus, *J. Amer. Chem. Soc.*, 1973, **95**, 6835.
[4] A. A. Reid, J. T. Sharp, H. R. Sood, and P. B. Thorogood, *J.C.S. Perkin I*, 1973, 2543, and refs. cited therein.
[5] M. Oki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc. Japan*, 1963, **36**, 1542; R. J. Kurland, M. B. Rubin, and W. B. Wyse, *J. Chem. Phys.*, 1964, **40**, 2426; F. G. Riddell and J. M. Lehn, *Chem. Comm.*, 1966, 375.