

## Stable 1,4-Dialkyl-1,4-dihydropyrazines

By J. W. LOWN\* and M. H. AKHTAR

(Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada)

**Summary** Stable  $8\pi$ -electron 1,4-dialkyl-1,4-dihydropyrazines are readily prepared by reaction of *N*-benzylidiphenacylamine hydrobromide with primary aliphatic amines provided the alkyl group has low migratory aptitude; proof of structure and ready oxidation to stable free radicals is discussed.

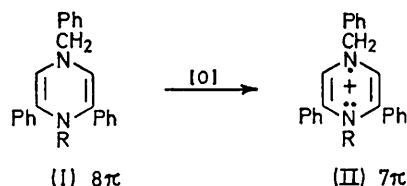
THE observation that 1,2-dihydropyrazines (resulting from the rearrangement of transient 1,4-dialkyl-1,4-dihydro-

pyrazines) may be isolated from the products of controlled thermal decomposition of 2-arylaziridines<sup>1</sup> led us to attempt the preparation of stable 1,4-dialkyl-1,4-dihydropyrazines which are of considerable interest in possessing potentially antiaromatic<sup>2</sup>  $8\pi$ -electron systems.

Although the action of benzylamine on *N*-benzylidiphenacylamine hydrobromide leads to the 1,2-dibenzyl-1,2-dihydropyrazine<sup>3,4</sup> by migration of the benzyl group, we now show that alkylamines, containing groups which are less

Treatment of *N*-benzylidiphenacylamine hydrobromide with two equivalents of cyclohexylamine under nitrogen in refluxing toluene afforded 4-benzyl-1-cyclohexyl-1,4-dihydro-2,6-diphenylpyrazine (I; R = cyclohexyl) as an orange solid (50%) m.p. 138—139.5°.‡ The simplicity of the n.m.r. spectrum is consistent with the  $C_{2v}$  symmetry of (I).

Catalytic hydrogenation of (I; R = cyclohexyl) at atmospheric pressure over Pd-C afforded the 1,2,3,4-tetrahydropyrazine (84%) as an oil.<sup>†</sup>



R = PhCH<sub>2</sub>CH<sub>2</sub>, Pr<sup>n</sup>, Bu<sup>n</sup>, Bu<sup>i</sup>, iso-C<sub>5</sub>H<sub>11</sub>, cyclo-C<sub>3</sub>H<sub>5</sub>, cyclo-C<sub>6</sub>H<sub>11</sub>.

The 1,4-dialkyl-1,4-dihydropyrazines are stable in the crystalline state but are reactive in solution (*e.g.* reaction as enamines towards  $\text{CHCl}_3$  and  $\text{CCl}_4$ ) and most significantly are readily oxidised by air to stable free radical cations which gave persistent e.s.r. signals and are tentatively

assigned to the radical cations (II). This sensitivity to oxygen results in considerable paramagnetic n.m.r. line broadening in the case of many of the 1,4-dialkyl-1,4-dihydropyrazines. Structure proof was however obtained with two additional representative examples (I; R = Bu<sup>n</sup>) (I; R = cyclopropyl) by catalytic hydrogenation to the 1,2,3,4-tetrahydro-compound the n.m.r. spectra of which were normal. The rapid oxidation of (I) by air parallels the similar behaviour of the structurally related 5,10-dihydro-phenazines<sup>6</sup> and phenoxazine.<sup>7</sup>

The e.s.r. spectra of II gave  $g$  values of 2.0025, close to the free electron value of  $g = 2.00232$ ,<sup>8</sup> indicative of an organic free radical and the spectrum width of (II; R = cyclopropyl) is  $6.25 \times 10^{-3}$  T resembling those previously obtained by the reduction in concentrated  $\text{H}_2\text{SO}_4$  solutions of the 6 $\pi$ -substituted pyrazines.<sup>9</sup>

The antiaromaticity inherent in structures (I) is evidently relieved by the rapid oxidation. Marked thermodynamic instability is implied for the 2,3-diphenyl-1,4-diethyl-1,4-dihydropyrazine postulated as a product of reduction by lithium aluminium hydride of the corresponding diacetyl compound.<sup>5</sup> Since the electron-withdrawing groups in the latter stabilise the 1,4-dihydropyrazine system it seems probable that the 1,4-dialkyl-1,4-dihydropyrazines described here owe their relative stability and isolability to restrictions on full  $\pi$ -conjugation possibly due to steric hindrance interactions at the 1, 2, and 6 positions.

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† Satisfactory analytical and u.v. spectroscopic data and exact mass measurement of the parent molecular ion peaks were obtained.

‡ A satisfactory n.m.r. spectrum was obtained.

<sup>1</sup> J. W. Lown and M. H. Akhtar, *Canad. J. Chem.*, in the press.

<sup>2</sup> R. Breslow, J. Brown, and J. Gajewski, *J. Amer. Chem. Soc.*, 1967, 89, 4383, R. Breslow, *Angew. Chem. Internat. Edn.*, 1968, 7, 565.

<sup>3</sup> S.-J. Chen and F. W. Fowler, *J. Org. Chem.*, 1970, **35**, 3987.

<sup>4</sup> A. T. Mason and G. R. Winder, *J. Chem. Soc.*, 1893, **63**, 1355.

<sup>b</sup> S.-J. Chen and F. W. Fowler, *J. Org. Chem.*, 1971, **36**, 4025.

<sup>6</sup> H. McIlwain, *J. Chem. Soc.*, 1937, 1704.

<sup>7</sup> D. E. Pearson, 'Heterocyclic Compounds', Wiley, New York, 1957, Vol. 6, Ch. 14.

<sup>8</sup> P. B. Ayscough in 'Electron Spin Resonance in Chemistry,' Methuen, London, 1967, p. 15.

\* J. R. Bolton, A. Carrington, and T. dos Santos-Veiga, *Mol. Phys.*, 1963, 5, 465; B. L. Barton and G. K. Fraenkel, *J. Chem. Phys.*, 1964, 41, 1455.