Suprafacial [1,3]-Sigmatropic Benzyl Shift in 1,4-Dibenzyl-1,4-dihydro-2,6-diphenylpyrazine

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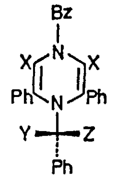
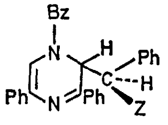
Summary The previously postulated intermediacy of 1,4-dibenzyl-1,4-dihydro-2,6-diphenylpyrazine (Ia) in the rearrangement to 1,2-dihydropyrazine (IIa) is demonstrated and the reaction proceeds in 95 ± 2% yield with first-order kinetics: crossover recombination experiments show only 12 ± 6% intermolecular contribution from a radical dissociation-recombination process which is prevented with butanethiol scavenger, and chiral (Id) rearranges in the presence of the scavenger with ⩾ 95% stereospecificity and with inversion of the migrating group indicating an 88 ± 6% component of a concerted [1,3]-sigmatropic shift with suprafacial allylic utilisation.

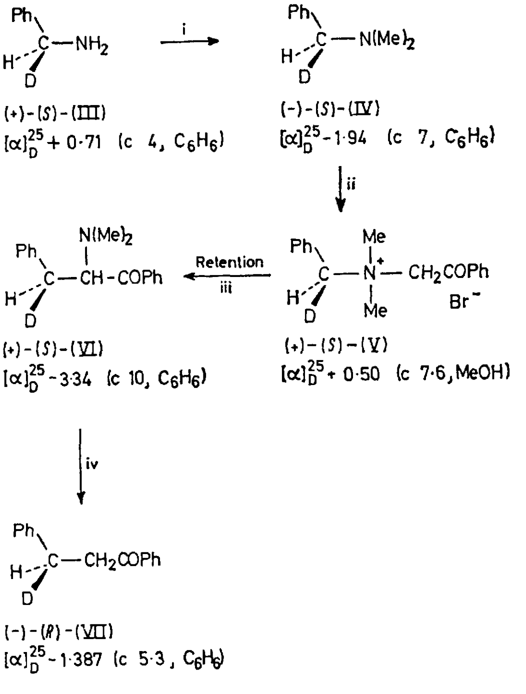
THE reaction of benzylamine with *N*-benzyldiphenacylamine hydrobromide, originally considered to afford a 1,4-dibenzyl-1,4-dihydropyrazine,[1] has been shown to give the 1,2-dibenzyl-1,2-dihydro-3,5-diphenylpyrazine and a 1,3-benzyl migration from the initially formed but unisolated 1,4-dibenzyl-1,4-dihydro-isomer was postulated.[2] We report that by employing lower reaction temperatures (40 ± 1°) it is possible to isolate the reactive intermediate (Ia)† as in the case of more stable 1,4-dialkyl-1,4-dihydropyrazines.[3] This isolation of (I) permitted confirmation of the postulated rearrangement and an examination of its mechanism which has a bearing on general 1,3-migrations.[4] Compound (Ia) rearranges in degassed benzene at 55° to (IIa) in ⩾95 ± 2% yield (determined spectroscopically) and obeys strictly first-order kinetics over 80% of the reaction, with $k = 6{\cdot}44 \pm 0{\cdot}4 \times 10^{-4}\ s^{-1}$ (in C_6H_6); $7{\cdot}95 \pm 0{\cdot}5 \times 10^{-4}\ s^{-1}$ (in THF), and $11{\cdot}80 \pm 0{\cdot}4 \times 10^{-4}\ s^{-1}$ (in o-$Cl_2C_6H_4$). The reaction thus shows a minimal dependence of rate on solvent polarity.



(I) a; X = Y = Z = H
b; X = D, Y = Z = H
c; X = H, Y = Z = D
d; X = H, Y = D, Z = H



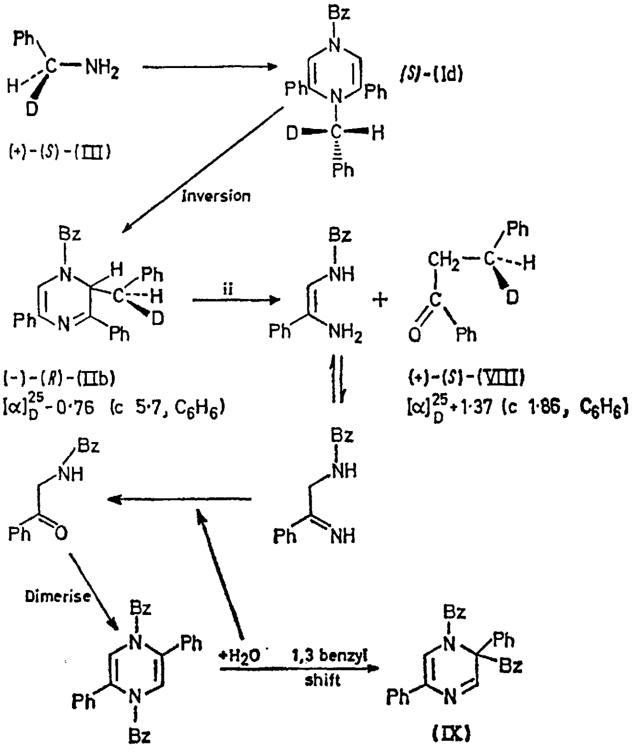
(II) a; Z = H
b; Z = D



SCHEME 1

i, $HCHO$–HCO_2H; ii, $PhCOCH_2Br$; iii, NaOH; iv, Zn–HOAc

To establish whether the reaction is intramolecular or intermolecular we performed a crossover recombination experiment. An intimate mixture (5 : 4) of (Ib) (80% deuterium incorporation) and of (Ic) (99·7% D incorporation) was rearranged at 80° in benzene. The isotopic content of labelled (II) (mass spectrometry) was consistent only with 12 ± 6% of (II) being formed by radical dissociation, crossover, and subsequent recombination. In the presence of the radical scavenger butanethiol, crossover was prevented completely. Similar experiments in hexane and tetrahydrofuran gave 14 and 12% crossover, respectively (the somewhat higher figure in the former solvent may reflect its lower viscosity[5]). These results suggest only a small extra-cage free-radical component and rule out a radical-chain process. No CIDNP effect[6] was detectable (which may be due to the low concentration of free radicals or to their limiting lifetime[7]).



SCHEME 2

i, Heat, C_6H_6; ii, Zn–HOAc, heat

To assess the degree of stereochemical integrity maintained during the rearrangement, the (*S*)-1,4-dibenzyl-1,4-dihydropyrazine (Id) was prepared from chiral (+)-(*S*)-benzyl[α-^{2}H]amine[8] (42% enantiomeric excess) and rearranged under identical conditions at 55° in benzene to give (IIb) $[\alpha]_D^{25}$ −0·68 ± 0·002 (*c*, 5·7, C_6H_6). When the reaction was repeated in the presence of butanethiol (which scavenges that portion of the rearranged product which is racemised in the extra-cage free-radical component) the product showed an increase specific rotation $[\alpha]_D^{25}$ −0·76 ± 0·002 (*c*, 5·75, C_6H_6). The configuration of the [α-^{2}H]-benzyl unit in (IIb) prepared in the presence of butanethiol was related to that in chiral 3-phenyl[3-^{2}H]propiophenone by a Stevens rearrangement (Scheme 1).

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† All new compounds gave satisfactory analytical and spectral data.

The Stevens rearrangement has recently been demonstrated to proceed by a radical dissociation–recombination mechanism by Schollkopf and others[9] and is known to proceed with $\geqslant 96\%$ retention for migration to Ph–CHMe.[9,10] The reasonable assumption is made that a similar retention obtains for migration of Ph–CHD– so the absolute configuration of (−)-(VII) is established.

Carefully controlled Zn-AcOH cleavage of (IIb) afforded a mixture of the desired chiral ketone (VIII) and the known isomeric 1,2-dihydropyrazine[11] (IX) in a ratio of 60:40 (n.m.r.). Compound (IX) plausibly arises as shown in Scheme 2. Chromatographic separation of (VIII) and (IX) on alumina gave (+)-(*S*)-3-phenyl[3-^{2}H]propiophenone (VIII) $[\alpha]^{25}_{D}$ $+1{\cdot}37 \pm 0{\cdot}002$ (*c*, 1·86, C_6H_6). Assuming 96% retention in the Stevens rearrangement then the specific rotation of (*R*)-(VII) with 42% enantiomeric excess would be $-1{\cdot}45° \pm 0{\cdot}002$. Therefore that part of the rearrangement of (I) to (II) ($88 \pm 6\%$) which proceeds intramolecularly proceeds with $\geqslant 95\%$ stereospecificity and with inversion of configuration which demands a [1,3]-sigmatropic shift with suprafacial allylic utilisation.[12]

As far as we are aware this represents the first clear-cut example of a [1,3]-sigmatropic shift with inverison involving nitrogen at the migrating centre. The rearrangement therefore proceeds by a combination of sigmatropic and dissociative mechanisms, and the contribution of the latter would be expected to be a function of the molecular environment and temperature. Baldwin and his co-workers have encountered several examples of dual competing mechanisms in the rearrangement of ylides.[13]

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