Optical Resolution of a Substituted 6,11-Diphenyldibenzo[*b,f*][1,4]diazocine and the Racemization Barrier

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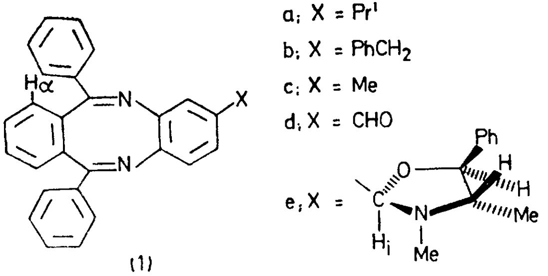
Summary 2-formyl-6,11-diphenyldibenzo[*b,f*][1,4]diazocine has been resolved into both optical isomers and the racemization barrier has been determined.

SUBSTITUTED 6,11-diphenyldibenzo[*b,f*][1,4]diazocines (**1**) possess a three-dimensional tub-like conformation (the eight-membered ring being a diazacyclo-octatetraene system) and as such are potentially resolvable into optically active forms. A value of at least 25 kcal mol^{-1} for the inversion barrier for compounds (**1**) would be expected from the effects on the inversion barrier of cyclo-octatetraene of non-bonded interactions in the transition state [1-4] and of fused benzene rings.[4,5] Compounds (**1**) should therefore be resolvable and stable enough to be handled.



(1)

The 60 MHz ^{1}H n.m.r. spectra ($CDCl_3$, Me_4Si, 35 °C) of (**1a**) and (**1b**) show accidental equivalence of the isopropyl methyl protons (δ 1·18, d, 6H) and of the benzyl methylene protons (δ 3·94, s, 2H) respectively. However, non-equivalences are observed for the isopropyl methyl groups in the ^{13}C n.m.r. spectrum of (**1a**): $\Delta\delta = 24{\cdot}27 - 24{\cdot}20 = 0{\cdot}07$ p.p.m. in $CDCl_3$ (Me_4Si reference) and $\Delta\delta = 23{\cdot}89 - 23{\cdot}61 = 0{\cdot}28$ p.p.m. in $(CD_3)_2SO$ {$\delta[(CD_3)_2SO = 39{\cdot}60$ p.p.m.}, confirming that no inversion occurs at 35 °C as predicted. The variation of $\Delta\delta$ with temperature [0·220, 0·187, and 0·120 p.p.m. at respectively 83, 110, and 150 °C in $(CD_3)_2SO$ might be due to temperature-dependent chemical shifts[4,6] (a complication of real significance for $\Delta G^{\ddagger}_c$ determinations) but it appears that no rapid inversion occurs at 150 °C.

The optical resolution of the aldehyde (**1d**), prepared from (**1c**), was attempted. Treatment of (**1c**)[7] with *N*-bromosuccinimide in CCl_4 in the presence of a catalytic amount of αα′-azobisisobutyronitrile[8] gave the corresponding bromide ($X = CH_2Br$, $Y = H$) which was directly oxidised by Me_2SO–HCO_3Na[9] to the aldehyde (**1d**),† m.p. 228—231 °C (overall yield 69%). The optical resolution of (**1d**) was performed by crystallisation of a chiral oxazolidine (**1e**) prepared from stoicheiometric amounts of (**1d**) and l-ephedrine in methylene chloride with molecular sieves at room temperature. It has already been shown[10] that only two diastereoisomers are formed during such a reaction, the asymmetric carbon atom which is created having the (*R*) configuration. This is confirmed by the 60 MHz ^{1}H n.m.r. spectrum of (**1e**) which shows only two singlets for the diastereotopic H_i protons (δ 4·60 and 4·65). One crystallisation of (**1e**) from light petroleum led to optically pure crystals: 19% yield, one singlet for H_i (δ 4·65), m.p. 157—160 °C, $[\alpha]^{25}_D - 58°$ ($CHCl_3$). After chromatography on silica gel, the optically pure aldehyde (**1d**) was recovered, m.p. 184—186 °C, $[\alpha]^{25}_D + 277°$ ($CHCl_3$, *c* 1·38).

Upon heating at 175 °C under nitrogen a partially optically active sample of the diazocine (**1d**) (optical purity 34%) dissolved in biphenyl, a slow racemization process was observed with $<$ 10% of thermal decomposition products being formed. The reaction was first order and the rate constant ($1{\cdot}14 \times 10^{-5}\ s^{-1}$), determined from the optical rotation of the recovered sample (purified by chromatography) led, from the Eyring equation, to: $\Delta G^{\ddagger} = 37$ kcal mol^{-1} (175 °C).

This result, the first reported value for the racemisation barrier of a dibenzodiazacyclo-octatetraene,‡ is consistent with strong nonbonded interactions between H_α and phenyl groups and with some loss of conjugation in the Ph–C=N units in the transition state.

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† Satisfactory elemental analyses were obtained for all new products. N.m.r. spectra were in agreement with the structure assigned.

‡ Until now only lower limits for racemization barrier of such systems have been reported[2,3] because the dibenzo[*e*,*g*][1,4]diazocines which were investigated decomposed before racemizing.

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