Conformation and Stereodynamics of *ortho*-Hydroxy and Ring-unsubstituted *N,N*-Dialkylbenzamides

W. Brian Jennings,* David Randall, and Barahman Movassagh Saket

Department of Chemistry, The University of Birmingham, P.O. Box 363, Birmingham B15 2TT, U.K.

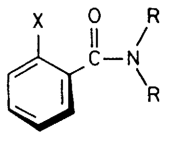
The non-equivalence of geminal groups in the low temperature n.m.r. spectra of 2-hydroxy-*N,N*-dialkylbenzamides and of the *ortho*-carbon atoms in 1-benzoyl-*cis*-3,5-dimethylpiperidine is indicative of a non-coplanar conformation with appreciable barriers ($\Delta G^{\ddagger}$ 7—9 kcal mol^{-1})† to rotation around the aryl–C(O) bond.

Rotation about the C(O)–N bond in amides has been extensively studied by n.m.r. spectroscopy. However, in the case of *ortho*-substituted *N,N*-dialkylbenzamides, [*e.g.* (**1**), R = Et; X = Me, NO_2, Cl, F], a second dynamic process has been observed which leads to the non-equivalence of geminal methylene protons in prochiral *N*-alkyl groups at *ca.* 0 °C.[1–3]

2-Hydroxybenzamides [(**1**), X = OH] are anomalous in that they are reported not to show geminal non-equivalence.[2] Furthermore the C(O)–N rotational barrier is somewhat lower than those of other *ortho*-substituted benzamides,[2,4] and i.r. spectra indicate a strong intramolecular hydrogen bond. These

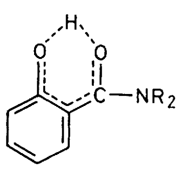
---

† 1 cal = 4.184 J.

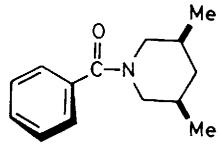


(1)

a; X = OH, R = Pr^i
b; X = H, R = Pr^i
c; X = OH, R = Et
d; X = OH, R = CH_2Ph



(2)



(3)

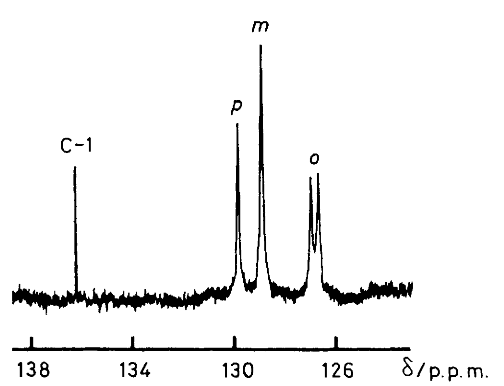


Figure 1. ^{13}C N.m.r. spectrum (aromatic region) of (**3**) at −95 °C in $CHCl_2F$ solution, recorded at 100.62 MHz.

observations have led to the suggestion that the formation of a six-membered chelate ring (**2**),[2] possibly with quasi-aromatic character,[4] leads to coplanarity of the aryl ring and the amide moiety.

We now report that some 2-hydroxybenzamides do in fact show geminal non-equivalence at low temperature. Specifically the di-isopropylamino compound (**1a**)[‡] shows non-equivalent isopropyl groups in the ^{1}H n.m.r. spectrum (100 MHz) below −40 °C owing to slow rotation around the amide bond ($\Delta G^{\ddagger}$ 11.8 kcal mol^{-1} at −38 °C). On further cooling both methyl doublets broaden again and at −110 °C are clearly split by a high field spectrometer (400 MHz) into four signals (δ 1.15, 1.23, 1.52, and 1.57) with approximately equal integrated intensity. This low temperature effect could in principle be due either to a frozen non-coplanar aryl ring (leading to diastereotopic geminal methyl groups) or to restricted rotation around the N–isopropyl bonds. Several examples of restricted N–isopropyl rotation in *N,N*-di-isopropylamides have been reported, but the spectral changes are quite different from those seen here in that two conformers were observed at low temperature with markedly different signal intensities.[5] Furthermore the analogous ring-unsubstituted benzamide (**1b**) shows only two methyl doublets (due to the *syn*-and *anti*-isopropyl groups) in the 400 MHz ^{1}H n.m.r. spectrum down to at least −130 °C. Accordingly the evidence is in favour of assigning the low temperature barrier in (**1a**) ($\Delta G^{\ddagger}$ 8.8 kcal mol^{-1} at −90 °C) to rotation of a non-coplanar aryl ring through the amide plane.

The diethyl and dibenzyl compounds (**1c**) and (**1d**) also showed a second dynamic process in the ^{1}H n.m.r. spectra at very low temperature (−120 to −150 °C), involving geminal anisochronism in one of the NCH_2 groups. Evidently the barrier to aryl–C(O) ring rotation in these less hindered di(primary alkyl)amides ($\Delta G^{\ddagger}$ *ca.* 7.5 kcal mol^{-1}) is appreciably lower than that in the di(secondary alkyl)amide (**1a**).

The absence of geminal non-equivalence in the low temperature spectra of the ring-unsubstituted compound (**1b**) does not necessarily imply that the phenyl ring is coplanar with the amide moiety or that rotation through the coplanar conformation ($\phi = 0°$) is always rapid on the n.m.r. time-scale since the orthogonal conformation ($\phi = 90°$) possesses a σ-plane containing the prochiral *N*-alkyl groups when X = H.[6] In order to investigate the situation in ring-unsubstituted benzamides we have prepared compound (**3**)[‡] which has appropriate stereochemistry to render the *ortho-* (and the *meta-*) protons or carbon atoms diastereotopic even when $\phi = 90°$. At ambient temperature the alkyl resonances of (**3**) split into *syn-* and *anti*-sets due to the normal slow rotation around the amide bond ($\Delta G^{\ddagger}$ 15.2 kcal mol^{-1} at 26 °C). However at much lower temperatures the two most intense signals in the ^{13}C n.m.r. spectrum broaden selectively and at −95 °C the upfield *ortho*-signal[7] was clearly resolved by a high field spectrometer into two equally intense components (Figure 1). To the best of our knowledge this is the first observation of restricted phenyl rotation in a ring-*unsubstituted* benzamide, and the barrier ($\Delta G^{\ddagger}$ 9.3 kcal mol^{-1} at −84 °C) to rotation through the amide plane § is appreciable, though as expected on steric grounds it is lower than that in other *ortho*-substituted benzamides[1–3] or ring-unsubstituted thiobenzamides.[8] *ortho*-Hydroxybenzamides are exceptional since the OH - - C=O interaction in the coplanar state is attractive, hence the aryl rotational barrier in (**1c**) is lower than (**3**). However the non-coplanarity of (**1a**—**c**) and (**3**) indicates that the repulsive interaction between the *ortho*-hydrogen atom and the neighbouring NR group is considerable.

We thank Dr O. Howarth and Dr E. Curzon, University of Warwick, for the high-field ^{1}H and ^{13}C n.m.r. spectra, and the S.E.R.C. for an allocation of time on this spectrometer.

Received, 25th January 1982; Com. 076

References

1 G. R. Bedford, D. Greatbanks, and D. B. Rogers, *Chem. Commun.*, 1966, 330; *ibid.*, 1967, 144.
2 A. H. Lewin and M. Frucht, *Tetrahedron Lett.*, 1970, 1079.
3 U. Berg and J. Sandström, *Tetrahedron Lett.*, 1976, 3197.
4 M. Hirota and K. Todokoro, *Chem. Lett.*, 1974, 777.
5 A. Lidén, C. Roussel, T. Liljefors, M. Chanon, R. E. Carter, J. Metzger, and J. Sandström, *J. Am. Chem. Soc.*, 1976, **98**, 2853; and references contained therein.
6 W. B. Jennings and M. S. Tolley, *Tetrahedron Lett.*, 1976, 695; W. B. Jennings, *Chem. Rev.*, 1975, **75**, 307.
7 See R. G. Jones and J. M. Wilkins, *Org. Magn. Reson.*, 1978, **11**, 20 for ^{13}C signal assignment in *N,N*-dialkylbenzamides.
8 U. Berg, *Can. J. Chem.*, 1977, **55**, 2297.

[‡] All new compounds gave satisfactory elemental analyses.

§ The ground state phenyl–C(O) twist angle (ϕ) in (**3**) is probably somewhat less than 90°. Thus an *X*-ray crystallographic study of 4-bromo-*N,N*-dimethylbenzamide, which may be considered to be nearly isosteric with (**3**), gave ϕ *ca.* 45° (R.P. Shibaeva, L. O. Atovmyan, and R. G. Kostyanovskii, *Dokl. Akad. Nauk SSSR*, 1967, **175**, 586). However oscillation through $\phi = 90°$ is expected to be a relatively facile process.