Rotational Isomerism of *NN'*-Dimethyl-α,ω-bis(benzoylamino)alkanes

Girolamo Cirrincione, Werner Hinz, and R. Alan Jones*
School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ

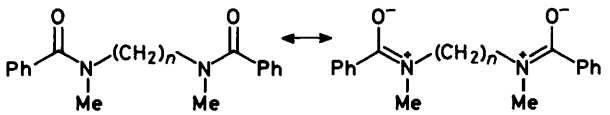
The low-temperature ^{1}H n.m.r. spectra of PhCO·N(Me)·$(CH_2)_n$·N(Me)·COPh show four signals for the methyl groups when $n \geqslant 3$, which are attributable to the presence of three rotational isomers. Only one isomer was detectable over a wide temperature range when $n = 2$. The rotational energy barriers have been measured and are close to that reported for *NN*-dimethylbenzamide.

In an extension of our studies on the synthesis of azafulvenes [1,2] we required a series of *NN'*-dimethyl-α,ω-bis(benzoylamino)-alkanes (**1**; R = Me). These compounds were readily obtained by methylation of the benzoylamines (**1**; R = H) with iodomethane in DMF under base-catalysed conditions. Examination of their ^{1}H n.m.r. spectra at *ca.* 20 °C showed two or three broad signals attributable to the methyl groups, together with a larger number of methylene group signals than were to be expected for the *NN'*-dimethyl derivatives. That the additional signals arose from rotational isomerism of the amide groups was confirmed by remeasurement of the spectra at 45 °C, when the spectra simplified to give the expected number of methyl and methylene signals. However, somewhat unexpectedly, when the ^{1}H n.m.r. spectra of (**1**; R = Me, n = 3—6) were measured at −20 °C, *four* resonance signals attributable to the *N*-methyl groups were observed (Table 1). Additionally, the signals for the *N*-methylene groups appeared as four overlapping triplets. It was not possible to resolve completely the signals for the methylene groups at 100 MHz, but discrete triplets for each of the *N*-methylene groups and multiple sets of signals for each of the non-nitrogen-bonded methylene groups were discernible when the spectra were measured at 400 MHz (Figure).

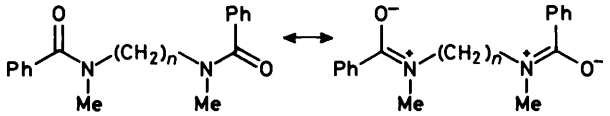
The appearance of the sets of four signals for the methyl groups and for each of the methylene groups may be interpreted in terms of the three rotational isomers (**2a**—**c**). Predictably, the symmetrical *ZZ*- and *EE*-isomers (**2a**, **c**) each gave rise to only one *N*-methyl signal at δ 3.09 ± 0.05 and 2.96 ± 0.01, respectively, whilst the *E,Z*-isomers (**2b**) produced two signals at δ 3.02 ± 0.01 and 2.86 ± 0.05, which can be assigned, respectively, to the methyl groups *trans* and *cis* to the carbonyl group. Confirmation of these assignments was provided by the observed chemical shifts for the two methyl group signals of *NN*-dimethylbenzamide and the single signal for the methyl group of the predominant conformer of *N*-methylbenzamide in which the methyl group is *cis* to the carbonyl group.

PhCO·NR·$(CH_2)_n$·NR·COPh

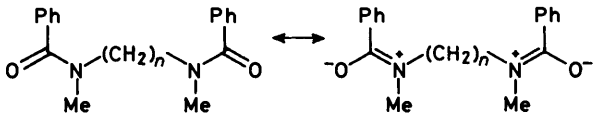
(1)



(2a)



(2b)



(2c)

It was noted that the disparity in the chemical shifts of the methyl signals for the *E,Z*-isomers with those of the methyl groups of the *E,E*- and *E,Z*-isomers having the same conformation was lessened with an increase in the alkane chain length and the signals for the methyl groups of the C_{12} compound could only be resolved at 400 MHz. This

Table 1. *N*-Methyl chemical shifts for *NN'*-dimethyl-α,ω-bis(benzoylamino)alkanes and related compounds

Compound	δ_{Me} at 253 K				δ_{Me} at 315 K	T_c ± 1/K	Δδ/Hz	Δ*G*/kJ mol^{-1}
NN-Dimethylbenzamide	3.092		2.949		2.968	301	14.2	65.1
(**1**; R = Me, n = 2)			2.948		3.036			
(**1**; R = Me, n = 3)	3.149	3.037	2.961	2.755	2.948	308	23.4	65.4
(**1**; R = Me, n = 4)	3.111	3.016	3.010	2.890	2.963	297	11.3	64.9
(**1**; R = Me, n = 5)	3.087	3.008	2.946	2.878	2.945	308.5	12.2	67.2
(**1**; R = Me, n = 6)	3.083	3.039	2.943	2.907	2.958	310	13.5	67.2
(**1**; R = Me, n = 12)	3.017[a]	3.013[a]	2.880		2.981	304	13.4	66.0
N-Methylbenzamide			2.928[b]		2.949[b]			
N-Methyl-α,ω-bis-(benzoylamino)dodecane	3.080		2.960		2.983	302	11.9	65.9

[a] Resolved at 400 MHz. [b] Doublet, *J* 4 Hz.

Table 2. ^{13}C N.m.r. chemical shifts [δ(p.p.m)] for *NN'*-dimethyl-α,ω-bis(benzoylamino)alkanes (**1**; R = Me) measured at *ca.* 20 °C

					Phenyl ring				
n	γ-CH_2	β-CH_2	α-CH_2	NMe	C-3,5	C-2,6	C-4	C-1	CO
2			44.4	37.8	126.7	128.3	129.4	136.2	171.8
3		24.6 26.0	44.8 48.8	32.8 37.3	126.5	128.2	129.2	136.4	171.2
4		24.0 25.2	46.7 50.7	32.7 37.3	126.6	128.3	129.3	136.5	171.2 171.4
5	23.4	26.5 27.7	46.9 50.8	32.6 37.3	126.6	128.2	129.2	136.6	171.1 171.2 171.7
6	26.0	26.7 27.9	47.2 50.9	32.5 37.3	126.6	128.2	129.1	136.6	171.1 171.4 171.6
12	*a*	*a*	47.4 51.1	32.6 37.6	129.9	127.9	129.5	136.8	171.7 171.0
$PhCONMe_2$				39.2 39.4	126.9	128.1	129.2	136.5	170.8

[a] Unresolved signals between 25.0 and 30.0 p.p.m.

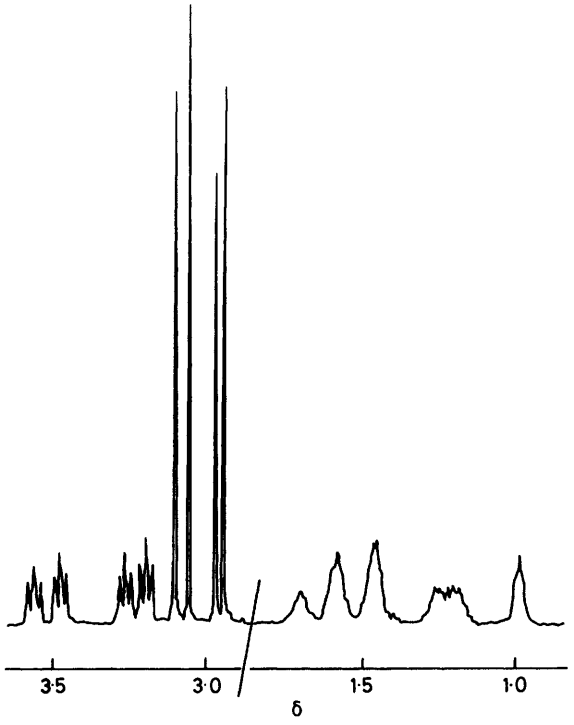
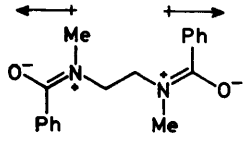


Figure. Methyl and methylene ^1H n.m.r. signals for *NN'*-dimethyl-α,ω-bis(benzoylamino)hexane measured at 400 MHz at −20 °C

observation is in accord with the expected difference in the across-space anisotropic effect of the amide groups upon the conformationally different methyl groups of the non-symmetrical *E,Z*-isomer, compared with the corresponding effect in the symmetrical *E,E*- and *Z,Z*-isomers. Similarly, the chemical shifts of the methylene groups of the *E,Z*-isomers approached those of the corresponding methylene groups of the *E,E*- and *Z,Z*-isomers as the alkane chain length was increased, but there was no significant change in the apparent coupling constants that could be linked with conformational changes in the alkane chain.

With the exception of the bis(benzoylamino)ethane (**1**; R = Me, *n* = 2), the relative stabilities of the three isomers are similar. There is no apparent stabilising or destabilising effect through dipole–dipole interactions of the amide groups and integration of the methyl signals at −20 °C showed, within experimental error, a statistical distribution of 1:2:1 for the *E,E*-, *E,Z*-, and *Z,Z*-isomers. One *N*-methylene singlet signal at δ 3.95 and one methyl signal at δ 2.95, compatible with the *E,E*-isomer, were predominant (>95%) in the spectrum of the bis(benzoylamino)ethane (**1**; R = Me, *n* = 2) over a temperature range of −40 to +40 °C. This observation is inconsistent with the data for the other compounds, but is compatible with a system which is stabilised by a strong dipolar interaction (**3**).



(3)

Measurement of the coalescence temperature of the methyl signals, T_c, allowed evaluation of the energy barrier to rotation of the amide groups.[3] The data presented in Table 1 show a close similarity to the rotational energy barrier for *NN*-dimethylbenzamide measured under comparable conditions and with literature values for other amides.[4] There was no significant systematic variation in the energy barrier with a change in the alkane chain length.

The ^{13}C n.m.r. spectra of the bisamides (Table 2) also showed multiplicity of the signals due to rotational isomerism, when the spectra were measured at 20 °C.

Experimental

100 MHz ^1H and ^{13}C n.m.r. spectra were measured for *ca.* 30% solutions in $CDCl_3$ using a JEOL FX-100 spectrometer. 400 MHz ^1H N.m.r. spectra were provided by the S.E.R.C high-resolution n.m.r. service at the University of Warwick and were measured using a Bruker WH-400 spectrometer. Variable-temperature n.m.r. spectral measurements were conducted using the JEOL FX-100 instrument, the temperatures being determined from the temperature-dependent chemical shift

Table 3. Bisbenzoyl derivatives of α,ω-diaminoalkanes and of α,ω-bis(methylamino)alkanes

n	Yield (%)	M.p. (°C)	Lit. m.p. (°C)		Analysis (%) C	H	N
PhCO·NH·$(CH_2)_n$·NH·COPh							
3	78	141—143	140[a]				
4	95	176—177	175—176[b]				
5	83	135—136	135—135.5[c]				
6	85	162—163	158—158.5[d]				
12	93	153	152—153[e]				
PhCO·NMe·$(CH_2)_n$·NMe·COPh							
2	91[f]	178	177—178[g]				
3	67	60		Required	73.5	7.1	9.0
				Found	73.5	7.15	9.0
4	45	117	116.5—117[h]				
5	54	*i*		Required	74.5	7.7	8.3
				Found	74.8	7.9	8.1
6	65[j]	68		Required	75.0	8.0	7.9
				Found	74.8	8.1	7.9
12	50	77		Required	77.0	9.2	6.4
				Found	77.1	9.3	6.4

[a] Ref. 5. [b] Ref. 6. [c] Ref. 7. [d] Ref. 8. [e] Ref. 9. [f] Obtained by benzoylation of α,ω-bis(methylamino)ethane. [g] Ref. 10. [h] Ref. 11. [i] Oil. [j] 86% yield obtained by benzoylation of α,ω-bis(methylamino)hexane.

differences of the signals for methanol contained in a closed capillary within the sample tube.[3]

Preparative t.l.c. separation of the acylated compounds was carried out on Kieselgel HF_{254} using diethyl ether–light petroleum (b.p. 60—80 °C) (1:1) as the eluant. Confirmation of the molecular weights of the methylated products was provided by mass spectral data obtained using a Kratos MS25 instrument.

General Procedure for the Benzoylation of α,ω-Diaminoalkanes.—Benzoyl chloride (2.81 g, 20 mmol) in dichloromethane (50 ml) was added dropwise to the α,ω-diaminoalkane (10 mmol) and triethylamine (2.0 g) in dichloromethane (100 ml) at 0 °C. The mixture was stirred at 15 °C for 2 h and the solvent was then removed under reduced pressure. The residue was washed with dilute hydrochloric acid (2 ml in 200 ml water) and saturated aqueous sodium carbonate (3 × 15 ml). Chromatographic elution of the product from silica with ethyl acetate gave the *NN'*-bisbenzoyl derivatives (Table 3).

Benzoylation of C_2 and C_6 α,ω-Bis(methylamino)alkanes.—The commercially available C_2 and C_6 α,ω-bis(methylamino)alkanes were benzoylated by a procedure analogous to that described for the benzoylation of the α,ω-diaminoalkanes.

General Procedure for the N-*Methylation of the C_2—C_6 α,ω-Bis(benzoylamino)alkanes.*—Potassium hydroxide (2.24 g, 40 mmol) was added to dimethylformamide (5 ml) with stirring. After 5 min, the bisamide (5 mmol) and iodomethane (2.84 g, 20 mmol) were added. The mixture was stirred at 15 °C for 4—6 h until no starting material remained (as shown by t.l.c analysis) and then poured into water (40 ml). The aqueous mixture was extracted with dichloromethane (3 × 10 ml) and the extracts were washed in succession with dilute aqueous hydrochloric acid (15 ml) and water (2 × 15 ml). Evaporation of the dried (Na_2SO_4) extracts gave oils, which upon chromatography from silica with ethyl acetate gave the *NN'*-dimethylamides (Table 3). Analytically pure samples were obtained by preparative t.l.c.

N-*Methylation of α,ω-Bis(benzoylamino)dodecane.*—Due to its poor solubility, the following modified procedure was used. The bisamide (2.0 g, 5 mmol) and iodomethane (2.84 g, 20 mmol) were added to potassium hydroxide (2.24 g, 40 mmol) in dimethylformamide (50 ml) and the mixture stirred at 30 °C for 12 h and then poured into water (100 ml). The aqueous mixture was extracted with dichloromethane (3 × 15 ml) and the extracts washed in succession with dilute aqueous hydrochloric acid (15 ml) and water (2 × 15 ml). Evaporation of the dried (Na_2SO_4) extracts gave a mixture of starting material and methylated compound. Extraction of the residue with ethanol (2 × 10 ml) left the unchanged starting material (80 mg, 4%) undissolved. Evaporation of the ethanolic solution and chromatography of the residue from silica with ethyl acetate gave the NN'-*dimethylbisamide* (Table 3) and N-*methyl*-α,ω-*bis(benzoylamino)dodecane* (87 mg, 42%), m.p. 66—67 °C (Found: C, 76.9; H, 9.2; N, 6.5. $C_{27}H_{38}N_2O_2$ requires C, 76.7; H, 9.1; N, 6.6%).

Acknowledgements

One of us (G. C.) thanks the NATO Scientific Affairs Division for a Fellowship and the University of Palermo for leave of absence.

References

1 C. F. Candy and R. A. Jones, *J. Chem. Soc. B*, 1971, 1405.
2 J. M. Brittain, R. A. Jones, R. O. Jones, and T. J. King, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2656.
3 J. Sandstrom, 'Dynamic NMR Spectroscopy,' Academic Press, London, 1982.
4 See, *e.g.*, L. M. Jackman, T. E. Kavanagh, and R. C. Haddon, *Org. Magn. Reson.*, 1969, **1**, 109; F. G. Riddell and D. A. R. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1973, 587; M. Davis, R. Lakhan, and B. Ternai, *J. Org. Chem.*, 1976, **41**, 3591.
5 S. R. Aspinall, *J. Am. Chem. Soc.*, 1941, **63**, 2843.
6 S. I. Kanevskaya, *J. Russ. Phys.-Chem. Soc.*, 1927, **59**, 639 (*Chem. Abstr.*, 1928, **22**, 2740).
7 S. I. Kanevskaya, *J. Russ. Phys.-Chem. Soc.*, 1927, **59**, 649 (*Chem. Abstr.*, 1928, **22**, 2141).
8 V. V. Korshak and S. R. Rafikov, *J. Gen. Chem. USSR* (*Engl. Transl.*), 1944, **14**, 974 (*Chem. Abstr.*, 1945, **39**, 4592).
9 V. Prelog and S. Polyak, *Helv. Chim. Acta*, 1957, **40**, 816.
10 L. Bauer, *J. Am. Chem. Soc.*, 1956, **78**, 1945.
11 E. J. Moriconi and A. A. Cevasco, *J. Org. Chem.*, 1968, **33**, 2109.

Received 19*th September* 1983; *Paper* 3/1642