NITROSUBSTITUTED 1,2-PHENYLENEDIAMINES

Concepción López [a,*], Maroš Bella[b], Viktor Milata[b,*], Rosa M. Claramunt[a]

Ibon Alkorta[c] and José Elguero[c]

[a]Departamento de Química Orgánica y Bio-Orgánica, Facultad de Ciencias, UNED, Paseo de Senda del Rey 9, E-28040 Madrid, Spain

[b]Department of Organic Chemistry, Institute of Organic Chemistry, Catalysis and Petrochemistry, Faculty of Chemical and Food Technology, Slovak University of Technology, Radlinského street 9, SK-81237 Bratislava, Slovak Republic

[c]Instituto de Química Médica, Centro de Química Orgánica Manuel Lora-Tamayo, CSIC, Juan de la Cierva 3, E-28006 Madrid, Spain

* Corresponding author. Tel.: + 34913987327; fax: + 34913988372.
E-mails: clopez@ccia.uned.es; viktor.milata@stuba.sk

Abstract

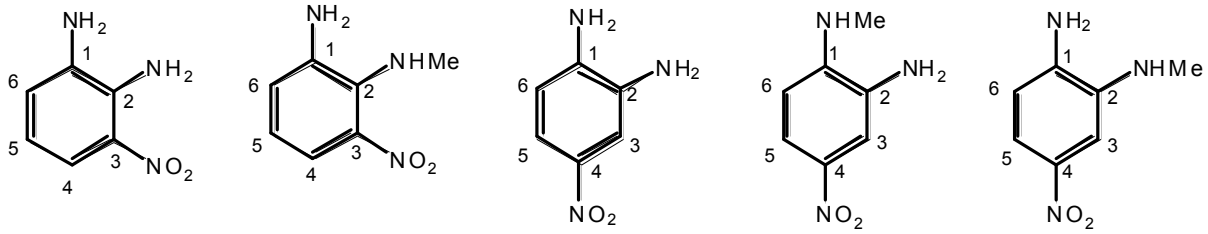
The ^{1}H, ^{13}C and ^{15}N NMR spectra, both in solution and in the solid state, of five 1,2-phenylenediamines have been recorded. Assignment of all the signals has been achieved and chemical shifts and coupling constants determined. When necessary homo- and heteronuclear 2D NMR experiments have been performed.

Keywords: aromatic amines, ^{1}H NMR, ^{13}C NMR, ^{15}N NMR

Introduction

The substituted 1,2-phenylenediamines are important precursors for the synthesis of nitrogen containing heterocycles such as benzimidazoles, benzotriazoles and benzodiazepines, among many others.[1,2] Moreover the importance of such heterocyclic systems in phamaceutical chemistry,[3] other commercial applications go from their use as hair dyes to the manufacture of diisocyanates.[4]

We present here the ^{1}H, ^{13}C, and ^{15}N NMR comparative studies of nitrosubstituted 1,2-phenylenediamines **1**-**5**, that were prepared by some of us[5,6] in view of their potential synthetic uses.



1 **2** **3** **4** **5**

Figure 1. Nitrosubstituted 1,2-phenylenediamines

Results and discussion

The results on the multinuclear NMR studies in solution are gathered in Tables 1 and 2, where all the ^{1}H and ^{13}C chemical shift assignments were made on the basis of their multiplicity, and taking into account the nitro and amino substituent effects. [7,8,9]

Table 1. ^{1}H NMR chemical shifts and some coupling constants of compounds **1-5** in DMSO-d_6

Comp.	H-3	H-4	H-5	H-6	Me	NHR-1	NHR-2
1	---	7.29 dd ^{3}J= 8.7 ^{4}J= 1.2	6.45 dd ^{3}J= 7.4 ^{3}J= 8.7	6.77 dd ^{3}J= 7.4 ^{4}J= 1.2	---	6.88 bs	5.20 bs
2	---	6.55 dd ^{3}J= 6.2 ^{4}J= 3.3	7.32 dd ^{3}J= 6.8 ^{3}J= 6.2	6.57 dd ^{3}J= 6.8 ^{4}J= 3.3	2.75 d ^{3}J = 4.8	7.02 bs	5.43 bs
3	7.38 d ^{4}J= 2.5	----	7.40 dd ^{3}J= 8.5 ^{4}J= 2.5	6.52 d ^{3}J= 8.5	---	6.00 bs	5.03 bs
4	7.39 d ^{4}J= 2.6	--	7.55 dd ^{3}J= 8.8 ^{4}J= 2.6	6.41 d ^{3}J= 8.8	2.83 d ^{3}J = 4.8	6.10 bs	5.06 bs
5	7.09 d ^{4}J= 2.5	----	7.48 dd ^{3}J= 8.7 ^{4}J= 2.5	6.55 d ^{3}J= 8.7	2.77 d ^{3}J = 4.9	6.09 bs	5.18 bs

bs: broad singlet; d: doublet

Table 2. ^{13}C and ^{15}N NMR chemical shifts in ppm and ^{1}H-^{13}C coupling constants in Hz of compounds **1–5** in DMSO-d_6

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	Me	NHR-1[a]	NHR -2[a]
1	131.1	135.1	137.8	113.0 ^{1}J= 167.2 ^{3}J= 8.7	115.7 ^{1}J= 163.0	117.2 ^{1}J= 165.0	---	−312.0	−324.4
2	130.6	135.7	138.9	112.2 ^{1}J= 167.2 ^{3}J= 8.7	115.9 ^{1}J= 164.2	111.9 ^{1}J= 158.4	30.4 ^{1}J= 135.7	−312.2 ^{1}J = 91.4	−328.8 ^{1}J = 91.3
3	143.3	133.9	108.1 ^{1}J= 161.4	136.8	115.6 ^{1}J= 166.8 ^{3}J= 4.6	111.5 ^{1}J= 160.0 ^{3}J= ^{3}J= 5.0	---	−310.8 ^{1}J = 89.3	−326.6 ^{1}J = 73.0
4	143.7	134.4	107.0 ^{1}J= 162.2	136.6	116.0 ^{1}J= 160.0 ^{3}J= 5.6	106.5 ^{1}J= 160.0 ^{3}J= 5.6	29.7 ^{1}J= 136.6	−315.0	−326.4
5	143.6	135.5	102.8 ^{1}J= 160.8	137.3	115.6 ^{1}J= 166.6 ^{3}J= 4.4	110.6 ^{1}J= 159.8	29.9 ^{1}J= 135.5	−310.8 ^{1}J = 86.5	−330.6 ^{1}J = 91.2

[a] Nitro groups were not detected as the ^{15} N NMR chemical shifts have been obtained by means of 2D (^{1}H–^{15}N) gs-HMQC experiments.

In the ^{1}H NMR spectra in DMSO-d_6, the amino group signals appear as broad singlets in all compounds, but when the 2D (^{1}H–^{15}N) gs-HMQC experiments were performed in order to detect the ^{15}N NMR chemical shifts of such groups, the ^{1}H NMR positive projection shows curious multiplicities in three compounds **2**, **3** and **5** as shown in Figures 2, 3 and 4, respectively.

The strange multiplicity of some signals (triplets, double triplets) could correspond to the anisochrony of N**H**$_2$ protons (restricted rotation due to the *p*-nitro groups). This phenomena is now under investigation, with the help of theoretical calculations.

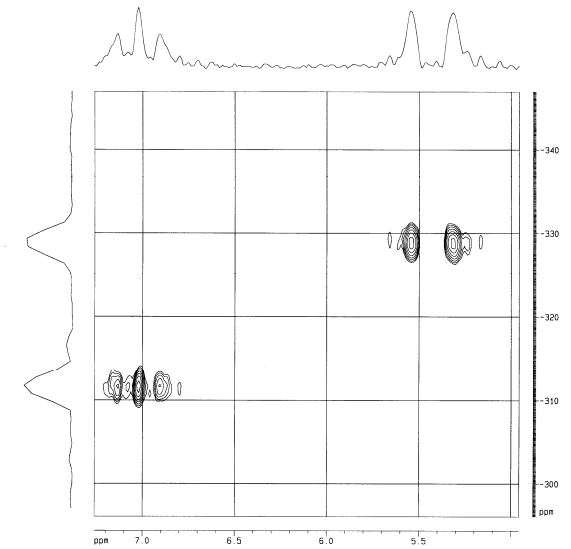


Figure 2. 2D (^{1}H–^{15}N) gs-HMQC spectra of compound **2**

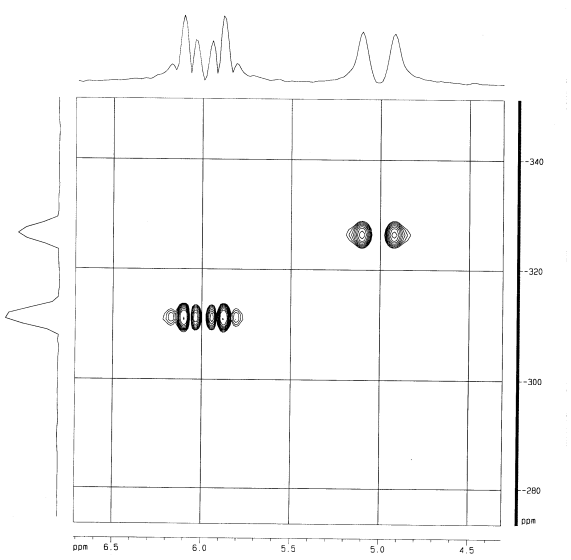


Figure 3. 2D (^{1}H–^{15}N) gs-HMQC spectra of compound **3**

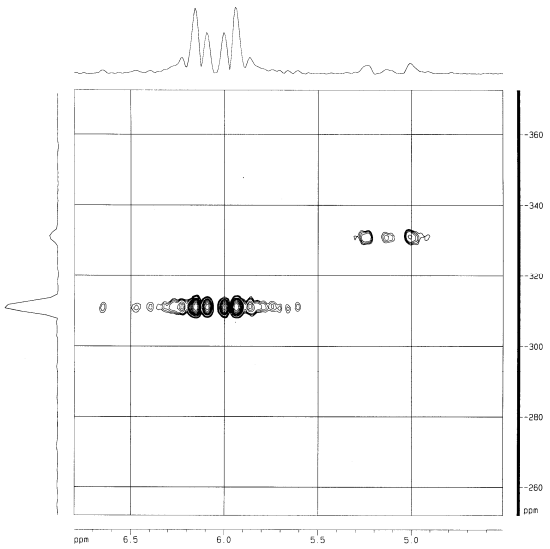


Figure 4. 2D (^{1}H–^{15}N) gs-HMQC spectra of compound **5**

The ^{13}C and ^{15}N NMR spectra of the five nitrosubstituted 1,2-phenylenediamines **1**-**5** were also recorded and the spectral regions assigned (Table 3) on the basis of the previous solution NMR studies. None ^{15}N NMR signal could be detected in the case of compound **3**, probably due to the substituent groups mobility in the polycrystalline sample.[10] In a similar way a broad signal was obtained for the NH_2-1, and the NO_2 was not observed, in the spectra of **5**. In the case of **2**, the nitrogens corresponding to the amino groups show two different chemical shifts for each of them, due to the existence of different independent molecules in the asymmetric unit cell.[11] As an example of the high resolution of the ^{13}C and ^{15}N CPMAS NMR signals, the spectra obtained for compound **4** are depicted in Figure 5.

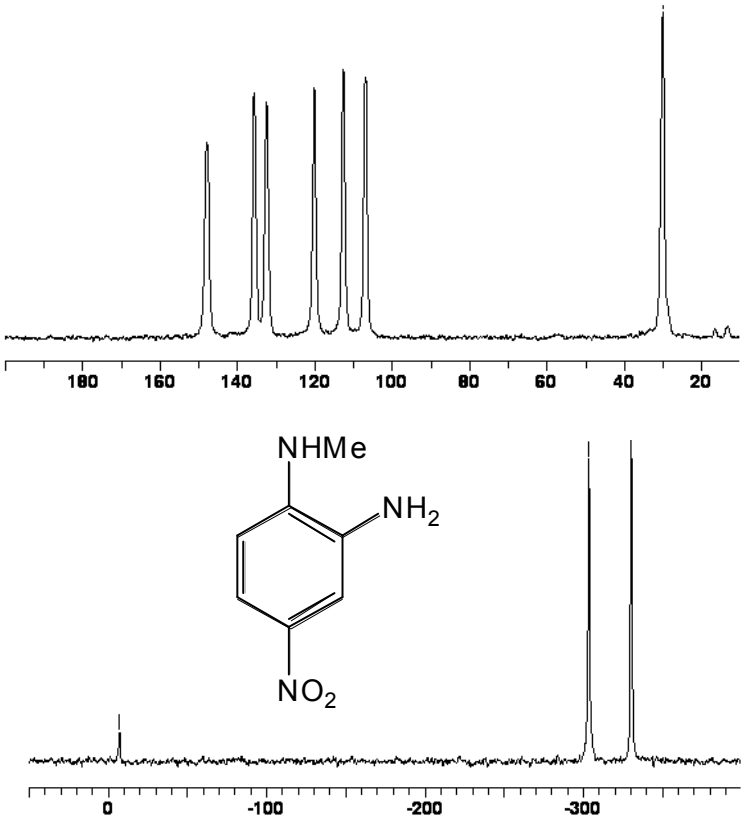


Figure 5. ^{13}C (upper part) and ^{15}N (low part) CPMAS NMR spectra of compound **4**

Table 3. ^{13}C and ^{15}N NMR CPMAS chemical shifts of compounds **1-5**

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	Me	NHR-1	NHR-2	NO_2
1	130.3	135.0	137.9	115.7	116.7	123.0	---	−303.3	−324.1	−3.9
2	130.0	138.7	138.7	115.8	115.8	111.7	31.7	−305.4 −308.7	−327.2 −331.6	−3.8
3	146.6	131.7	111.8	134.9	119.8	113.7	---	nd	nd	nd
4	147.8	132.3	112.5	135.5	120.0	106.8	30.0	−303.5	−330.3	−7.2
5	142.7	139.6	102.6	137.5	114.3	114.3	30.7	~−310 (b)	−326.7	nd

nd: not detected signal; b: broad signal

Experimental Procedure

NMR spectroscopy

Solution spectra were recorded at 300 K on a Bruker DRX 400 (9.4 Tesla, 400.13 MHz for ^{1}H, 100.62 MHz for ^{13}C and 40.56 MHz for ^{15}N) spectrometer with a 5-mm inverse detection H–X probe equipped with a z-gradient coil for ^{1}H, ^{13}C and ^{15}N, save specified. Chemical shifts (δ in ppm) are given from internal solvent, DMSO-d_6 (2.49) for ^{1}H and DMSO-d_6 (39.5) for ^{13}C. And external reference $CH_3{}^{15}NO_2$ (0.00) for ^{15}N NMR was used. 2D (^{1}H–^{1}H) gs-COSY and inverse proton detected heteronuclear shift correlation spectra, (^{1}H–^{13}C) gs-HMQC, (^{1}H–^{13}C) gs-HMBC, (^{1}H–^{15}N) gs-HMQC, were acquired and processed using standard Bruker NMR software and in non-phase-sensitive mode.[12] Gradient selection was achieved through a 5% sine truncated shaped pulse gradient of 1 ms. Variable temperature experiments were recorded on the same spectrometer. A Bruker BVT3000 temperature unit was used to control the temperature of the cooling gas stream and an exchanger to achieve low temperatures.

Solid state ^{13}C (100.73 MHz) and ^{15}N (40.60 MHz) CPMAS NMR spectra have been obtained on a Bruker WB 400 spectrometer at 300 K using a 4 mm DVT probehead and a 4-mm diameter cylindrical zirconia rotor with Kel-F end-caps. The non-quaternary suppression (NQS) technique to observe only the quaternary carbon atoms was employed.[12] ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to the Me_4Si (for the carbonyl atom δ (glycine) = 176.1 ppm) and ^{15}N spectra to $^{15}NH_4Cl$ and then converted to nitromethane scale using the relationship: δ ^{15}N(nitromethane) = δ ^{15}N(ammonium chloride) – 338.1 ppm.

Acknowledgments

This work is supported by Grants CTQ2007-62113 and CTQ2010-16122 (Ministerio de Ciencia e Innovación, MICINN, Spain).

References

[1] A. R. Katritzky, Ch. A. Ramsden, E. F. V. Scriven, R. J. K. Taylor (Editors), *Comprehensive Heterocyclic Chemistry III*, 15 volume set, Elsevier, **2008**.
[2] M. A. García, R. M. Claramunt, T. Solčan, V. Milata, I. Alkorta, J. Elguero, ^{13}C and ^{15}N NMR spectra of aminobenzimidazoles in solution and in the solid state, *Magn. Reson. Chem*. **2009**, *47*, 100-104.
[3] D. J. Abraham, D. P. Rotella (Editors), *Burgers Medicinal Chemistry, Drug Discovery and Development*, 8 volume set, Wiley, **2010**.
[4] R. W. Layer, Amines, Aromatic, Phenylenediamines, *Kirk-Othmer Encyclopedia of Chemical Technology*, Wiley, **2000**.
[5] M. Bella, V. Milata, New route for preparation of nitrosubstituted 1,2-phenylene diamines, *J. Heterocycl. Chem*. **2008**, *45*, 425-427.

[6] M. Bella, V. Milata, L. I. Larina, 2-Amino-X-nitrobenzimidazoles as precursors of food borne carcinogens: A new approach to IQ synthesis, *J. Heterocycl. Chem*. manuscript in press.
[7] E. Pretsch, Th. Clerc, J. Seibl, W. Simon, *Tablas para la determinación estructural por métodos espectrscópicos*, Springer-Verlag Ibérica, **1998**.
[8] E. Breitmeier, W. Voelter, *Carbon-13 NMR Spectroscopy*, 3rd edn, VCH, Weinheim, **1987**.
[9] S. Berger, S. Braun, H.-O. Kalinowski, *NMR Spectroscopy of the non-metallic elements*, Wiley, New York, **1997**.
[10] R. K. Harris, R. E. Wasylishen, M. J. Duer (Editors), *NMR crystallography*, Wiley, Chichester, **2009**.
[11] G. P. A. Yap, R. M. Claramunt, C. López, M. A. García, C. Pérez-Medina, I. Alkorta, J. Elguero, The structures of chiral and racemate campho[2,3-c]pyrazole: a combined crystallographic, solid-state NMR and computational study, *J. Mol. Struct.* **2010**, *965*, 74.
[12] S. Berger, S. Braun, *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**.