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Intramolecular Hydrogen Exchange in *N*-(2,4-Dinitrophenyl)-1,3-diamino-2,2-dimethylpropane and Related Compounds

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By comparison of the NMR spectrum of the title compound with that of the analogous compound carrying a terminal dimethylamino group instead of an amino group, intramolecular hydrogen exchange has been demonstrated to take place between the two different nitrogen atoms in these substances. By varying the degree of nitro substitution in the aromatic ring, the rate of the exchange can be varied.

The NMR spectrum of *N*-(2,4-dinitrophenyl)ethylenediamine has been studied previously.[1] A rapid intramolecular nucleophilic substitution *via* a spirocyclic Meisenheimer complex was expected. Although no evidence for such a reaction was found, the possibility of its occurring at a lower rate than could be observed with the experimental method used (NMR) still remains to be investigated.

A different kind of reaction that may occur with *N*-(2,4-dinitrophenyl)ethylenediamine and similar compounds is hydrogen exchange between the amino groups. In particular, the intramolecular exchange between the "inner" and the "outer" amine protons seemed to be an interesting possibility. The presence of nitro groups in the aromatic ring makes the "inner" amino group acidic,[2] whereas the "outer" amino group is basic. With a suitable number of methylene groups joining the two amino groups, a cyclic mechanism for proton transfer can be postulated, as is indicated in Fig. 1.

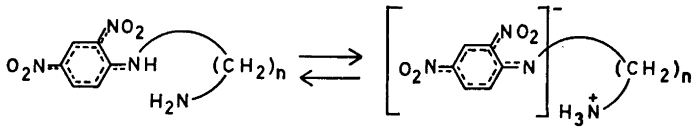


Fig. 1. Intramolecular mechanism for hydrogen exchange in 2,4-dinitrophenyl substituted polymethylenediamines.

In a recent kinetic study of base catalysis in the reactions between 2,6-dinitroanisole and a series of polymethylenediamines having different chain lengths, Palmertz and Lamm [3] found no evidence of intramolecular base catalysis, which had been assumed to operate as illustrated in Fig. 2. This

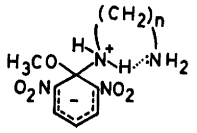
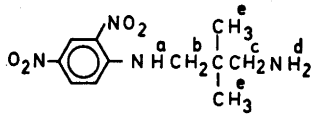


Fig. 2. Structure allowing intramolecular base catalysis in nucleophilic aromatic substitution with polymethylenediamines.

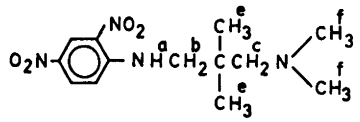
result, however, does not rule out the possibility of intramolecular hydrogen transfer, since the absence of intramolecular base catalysis in the above mentioned reactions may have other causes.

In the present work NMR spectroscopy was used as a tool to detect hydrogen exchange. It is known [4,5] that the methyl group in *N*-methylanilines, substituted with one or more nitro groups in the *ortho* and *para* positions, appears as a doublet in the NMR spectrum because of spin coupling with the amine proton. In this connection, it has been observed that this coupling is broken if a suitable base, *e.g.*, an aliphatic amine, is added to the system. Clearly, then, the terminal amino group in *N*-(2,4-dinitrophenyl)-ethylenediamine might be basic enough to make hydrogen exchange possible.

The compound *N*-(2,4-dinitrophenyl)ethylenediamine was not well suited to the present investigation. In the absence of further coupling, its methylene protons form an AA'BB' system, and additional coupling from the "inner" amino proton creates a rather complex situation. (The "outer" amino protons are probably involved in fast intermolecular exchange and, in consequence, will not contribute). For simplicity, it was decided to carry out the present investigation with a compound containing a neopentyl-like side chain, namely, *N*-(2,4-dinitrophenyl)-1,3-diamino-2,2-dimethylpropane (I in Fig. 3).



I



II

Fig. 3. Structure of compounds studied in the present work.

Some predictions can be made about the NMR spectrum of this compound. If it is assumed that no rapid exchange (in the NMR time scale) involving the *a* protons takes place (see Fig. 3), spin coupling between the *a* and *b* protons will cause the *b* protons to appear as a doublet. If, however, the *a* protons are involved in rapid exchange, either intra- or intermolecular, the coupling between *a* and *b* is broken, and the *b* protons should form a singlet. The *c* protons will probably appear as a singlet because of intermolecular exchange of the *d* protons (a general phenomenon with aliphatic amines).

It is possible, at least in theory, to suppress the rates of all intermolecular processes by dilution, leaving the intramolecular rates unaffected. If intermolecular exchange had been the only mechanism of exchange in I, the *b* protons would eventually appear as a doublet. From an experimental point of view, however, dilution is restricted to a rather narrow range, since the NMR method is not a very sensitive one.

An alternative method of approaching the question of the exchange mechanism is provided by comparison with compound II in Fig. 3. The terminal amino group in I is replaced by a dimethylamino group which carries no protons. There is no great difference in basicity between primary and tertiary amines. Recalling that basicity is a measure of the ability to accept a proton we may assume that any exchange process between the two nitrogen atoms in I will occur at a comparable rate in II under the same conditions. An intramolecular proton transfer in II will yield a tautomeric form in which the proton is situated at the terminal amino group. When this form reconverts to II, it is *the same* proton that becomes attached to the inner nitrogen atom. The spin coupling between *a* and *b* is therefore not broken, and *b* will appear as a doublet. If *b* should prove to be a singlet, intermolecular exchange must take place at a sufficiently high rate to cause the loss of identity of *a*.

For reasons that will become apparent below, it proved advantageous to prepare the *ortho* nitro compound analogous to I.

EXPERIMENTAL

Melting points have been determined on a Kofler micro hot stage.

1,3-Dinitro-2,2-dimethylpropane was prepared from acetone and nitromethane using diethylamine as a catalyst.[6] Yield 56 %, b.p. found 120–122°C/2 mm, lit.[6] 130–132°C/10 mm.

1,3-Diamino-2,2-dimethylpropane has earlier been prepared from the preceding compound by hydrogenation over Raney nickel at 20°C and 42 atm. initial pressure. The reduction was found to work equally well at an initial pressure of 4 atm., the other conditions being the same. Yield 45 %, b.p. found 154°C, lit.[6] 154–156°C.

N-(2-Nitrophenyl)-1,3-diamino-2,2-dimethylpropane * was prepared from 1.0 g (0.0071 mole) of 2-nitrofluorobenzene and 3.6 g (0.035 mole) of 1,3-diamino-2,2-dimethylpropane in 50 ml of methanol by keeping the solution at room temperature for 3 days. The solvent and excess of 1,3-diamino-2,2-dimethylpropane were removed *in vacuo* (2 mm), and the remainder was dissolved in ether. The ether solution was washed twice with water, dried over Drierite, and the ether was removed *in vacuo*. The product is a red oil at room temperature, but solidifies completely when placed in a freezer at −15°. The structure of the compound was verified by NMR. Yield 1.3 g (82 %).

* Compounds marked with an asterisk are believed to be new.

N-2,4-Dinitrophenyl-1,3-diamino-2,2-dimethylpropane * was prepared from 1.0 g (0.0051 mole) of 2,4-dinitroanisole and 2.6 g (0.026 mole) of 1,3-diamino-2,2-dimethylpropane in 50 ml of methanol by keeping the solution at room temperature for 24 h. The solvent and excess of 1,3-diamino-2,2-dimethylpropane were removed *in vacuo*, (2 mm), and the remainder was recrystallized three times from carbon tetrachloride. Yield 1.1 g (81 %), m.p. found 108–110°C. The structure was verified by NMR.

3-Dimethylamino-2,2-dimethylpropanal was prepared according to Brannock *et al.*[7] Yield 52 %, b.p. found 36–38°C/10 mm, lit.[7] 57–59°C/26 mm.

3-Dimethylamino-2,2-dimethylpropanal oxime was prepared from 120 g (0.93 mole) of the preceding compound and 75 g (1.09 mole) of hydroxylammonium chloride in 200 ml of water by keeping at room temperature for 24 h. Addition of sodium hydroxide solution caused the precipitation of the oxime as white crystals. These were filtered off, washed with water, dried, and recrystallized from petroleum ether (40–60°C) to yield 119 g (89 %) of pure product. M.p. found 54°C, lit.[8] 57°C.

3-Amino-1-dimethylamino-2,2-dimethylpropane was prepared by hydrogenation of 15.0 g (0.104 mole) of the above oxime with 10 g of Raney nickel in 200 ml of methanol in a low-pressure Parr hydrogenator at an initial pressure of 4 atm. The solvent was evaporated and the product distilled *in vacuo*. Yield 6.7 g (49 %), b.p. found 45–46°C/14 mm, lit.[9] 155–158°C, 70°C/12 mm. (The b.p. 70°C/12 mm is probably incorrect).

N-(2,4-Dinitrophenyl)-N′,N′-dimethyl-1,3-diamino-2,2-dimethylpropane * was prepared from 1.0 g (0.0051 mole) of 2,4-dinitroanisole and 2,0 g (0.015 mole) of 3-amino-1-dimethylamino-2,2-dimethylpropane in 50 ml of methanol by keeping the solution at room temperature for 24 h. The solvent and excess of 3-amino-1-dimethylamino-2,2-dimethylpropane were removed *in vacuo*, (2 mm). The remaining material was pure according to NMR and could be used directly. Yield 1.3 g (87 %), m.p. found 112–113°C.

NMR spectral experiments. The instrument used was a Varian A-60 spectrometer. The probe temperature was 38 ± 1°C. The nitrosubstituted monoaryl compounds prepared above were studied in two solvents, nitrobenzene and deuterochloroform. In nitrobenzene solution, the spectrum of *N*-(2,4-dinitrophenyl)-1,3-diamino-2,2-dimethylpropane was recorded at several different concentrations, namely 9.7, 4.7, 2.6, 1.1, and 0.6 % by weight. In all other cases, the spectra were recorded at two different concentrations, 10 and 5 % by weight. In no case was any significant concentration dependence observed for the chemical shifts and other properties.

RESULTS

The chemical shifts and coupling constants obtained for the three compounds studied are presented in Tables 1 and 2 (nitrobenzene and deuterochloroform solution, respectively). The "inner" amino protons could not be observed, either because their NMR signals were too broad or because they were swamped by solvent signals (in the case of nitrobenzene), or both.

DISCUSSION

The only case in which no coupling between the "inner" amino proton and the adjacent methylene protons is observed is represented by compound I in nitrobenzene solution (Table 1). This case is indicative of exchange involving the "inner" amino protons. The *b* signal in II is a doublet. In view of the introductory discussion, it can be concluded that an exchange of protons between the "inner" and "outer" nitrogen atom *does* take place in this type of compounds, and that it is intramolecular. These findings are naturally qualitative rather than quantitative, but they are nevertheless sufficient for the purpose of the present work. The fact that *N*-(2-nitrophenyl)-1,3-diamino-2,2-dimethylpropane does not show evidence of exchange in the NMR time

Table 1. NMR chemical shifts (δ) and coupling constants (J) in nitrobenzene solution. Singlets and doublets are denoted by (s) and (d), respectively. Chemical shifts are given in ppm downfield from TMS and are accurate to ± 0.02 ppm. The coupling constants are given in Hz and are accurate to ±0.2 Hz. The subscripts *a*, *b* etc. in the column headings refer to the corresponding protons in Fig. 3.

Compound	δ_b	δ_c	δ_d	δ_f	δ_e	J_{ab}
2-Nitro, terminal amino	3.17(d)	2.70(s)	1.53(s)	—	1.03(s)	5.1
2,4-Dinitro, terminal amino	3.35(s)	2.78(s)	1.60(s)	—	1.08(s)	—
2,4-Dinitro, terminal dimethylamino	3.47(d)	2.38(s)	—	2.38(s)	1.03(s)	4.5

scale demonstrates that, in this compound, the "inner" amino group is not acidic enough to permit rapid exchange of its proton.

An alternative explanation of the difference in the appearance of the *b* protons in I and the corresponding protons in the 2-nitro compound in nitrobenzene solution is that the compounds are not absolutely pure. A basic impurity in I might cause rapid exchange of the *a* protons, leading to a *b* singlet. Since, however, the NMR spectrum of I was unchanged upon repeated recrystallization, this explanation appears very unlikely. Furthermore, deliberate addition of a basic catalyst to the 2-nitro compound would then have been expected to give rise to a singlet for the "inner" methylene protons.

Table 2. NMR chemical shifts (δ) and coupling constants (J) in deuterochloroform solution. Singlets and doublets are denoted by (s) and (d), respectively. Chemical shifts are given in ppm downfield from TMS and are accurate to ±0.02 ppm. The coupling constants are given in Hz and are accurate to ±0.2 Hz. The subscripts *a*, *b* etc. in the column headings refer to the corresponding protons in Fig. 3.

Compound	δ_b	δ_c	δ_d	δ_f	δ_e	J_{ab}
2-Nitro, terminal amino	3.20(d)	2.67(s)	1.23(s)	—	1.03(s)	5.0
2,4-Dinitro terminal amino	3.33(d)	2.73(s)	1.28(s)	—	1.07(s)	5.0
2,4-Dinitro, terminal dimethylamino	3.43(d)	2.52(s)	—	2.47(s)	1.12(s)	4.5

In a check experiment, where a minute amount of the strongly basic and weakly nucleophilic catalyst sodium *t*-amylate was added to the NMR sample, no change in the spectrum was observed. The alternative explanation can therefore be ruled out.

In the introductory part, it was suggested that the terminal amine protons in I are involved in rapid intermolecular exchange. This is, in fact, demonstrated in the NMR spectra; in *all* cases. the "outer" methylene protons appear as a singlet.

In the dilution experiment performed with compound I in nitrobenzene solution, no changes in the *b* signal could be observed. In view of the narrow range of concentration studied, this experiment cannot be given too much weight, but it does lend additional support to the intramolecular exchange mechanism.

Surprisingly, compound I did not show evidence of exchange involving the "inner" protons in deuterochloroform solution (Table 2). This difference may be purely quantitative, the rate being lower in chloroform than in nitrobenzene. Since no large changes in any of the chemical shifts, in particular those of the amine protons, were observed (Tables 1 and 2), a more specific interaction between solvent and solute seems unlikely.

In conclusion, the mechanism proposed in Fig. 1 for intramolecular proton transfer is assumed to operate.

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REFERENCES

1. Lamm, B. *Acta Chem. Scand.* **19** (1965) 1492.
2. Stewart, R. and O'Donnell, J. P. *J. Am. Chem. Soc.* **84** (1962) 493.
3. Palmertz, I. and Lamm, B. *Acta Chem. Scand.* **23** (1969) 3361.
4. Heidberg, J., Weil, J. A., Janusonis, G. A. and Anderson, J. K. *J. Chem. Phys.* **41** (1964) 1033.
5. Lamm, B. *Acta Chem. Scand.* **19** (1965) 2316.
6. Lambert, A. and Lowe, A. *J. Chem. Soc.* **1947** 1517.
7. Brannock, K. C., Burpitt, R. D., Davis, H. E., Pridgen, H. S. and Thweatt, J. G. *J. Org. Chem.* **29** (1964) 2579.
8. Mannich, C., Lesser, B. and Silten, F. *Ber.* **65** (1932) 378.
9. *Beilsteins Handbuch der Organischen Chemie*, 4th Ed., 3rd Supplement, vol. IV, p. 596.

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