n.m.r.: 2.32 (s, $2CH_3$), 3.57 (q, CH_2), 4.20 (m over s, 8FcH), 5.89 (s, CH), 6.37 (m, OH), 7.95 δ (m, 5 benzene H).

Anal. Calcd. for $C_{20}H_{23}FeNO$: C, 68.78; H, 6.64; N, 4.01; Fe, 15.99. Found: C, 68.74; H, 6.63; N, 3.97; Fe, 16.20.

2-(α-Phenylhydroxymethyl)-1-(hydroxymethyl)ferrocene (3)

The methiodide of **2** (0.322 g) was placed in 35 ml of 1 *N* potassium hydroxide solution, refluxed for 5 h, and filtered hot. After cooling, the solution was extracted with ether and the ether layer was washed with water, dried, and concentrated to give **3**, m.p. 117–118° from benzene–heptane; i.r. (KBr): 3325, 1115, 1005 cm^{-1}.

Anal. Calcd. for $C_{18}H_{18}FeO_2$: C, 67.10; H, 5.63. Found: C, 67.35; H, 5.81.

2-(β-Hydroxyethyl)-N,N-dimethylaminomethylferrocene (4)

N,N-Dimethylaminomethylferrocene (20.0 g, 82.4 mm) in 100 ml of diethyl ether was lithiated with 41.0 ml (103 mm) of *n*-butyllithium in hexane. After lithiation was complete, 14.4 g (0.33 mol) of ethylene oxide in 25 ml of diethyl ether was added dropwise with cooling. After the addition was complete the reaction mixture was allowed to warm to room temperature and stirred for 9 h. Water and 10% sodium thiosulfate solution were added and a large amount of polymeric material separated. The ether layer and ether washes of the reaction mixture were combined and extracted with 1:10 phosphoric acid. The acid extracts were added dropwise to 20% sodium carbonate solution and the resultant oil extracted with ether. The dried ether extract was concentrated to give an oil which was chromatographed on alumina to give 6.85 g of starting ferrocene and 5.86 g of *4* as a yellow oil; i.r. (neat): 3400, 3100, 1110, 1005 cm^{-1}. The yellow oil gave a hydrochloride, m.p. 165° (darkens from 145°); i.r. (KBr): 3300, 3100, 2650, 1110, 1005 cm^{-1}.

Anal. Calcd. for $C_{15}H_{22}ClFeNO$: C, 55.66; H, 6.85; N, 4.33. Found: C, 55.77; H, 6.92; N, 4.30.

1. D. W. Slocum, B. W. Rockett, and C. R. Hauser. J. Am. Chem. Soc. **87**, 1241 (1965).
2. F. D. Popp and E. B. Moynahan. J. Org. Chem. **34**, 454 (1969).
3. F. D. Popp and E. B. Moynahan. J. Heterocycl. Chem. **7**, 739 (1970).

Revisions of Structural Assignments for 1-Methyl-(3 and 5)-amino-4-nitropyrazoles and Related Compounds

Misbahul Ain Khan and Brian M. Lynch
Organic Chemistry Laboratory, St. Francis Xavier University, Antigonish, Nova Scotia

Received July 5, 1971

Amino proton chemical shifts recorded for the compounds described as 5-amino-1-methyl-4-nitropyrazole and the 3-amino isomer (3) are inconsistent with charge densities calculated from simple H.m.o. treatments.

Unequivocal synthesis of 5-amino-1-methyl-4-nitropyrazole from 5-amino-1-methylpyrazole proves that the assignments should be interchanged; the structures of compounds derived from these aminonitropyrazoles are revised accordingly.

Les déplacements chimiques des protons amino du composé décrit comme étant l'amino-5 méthyl-1 nitro-4 pyrazole ainsi que de l'isomère amino-3 (3), ne sont pas compatibles avec les densités de charge calculées par simple traitement H.m.o.

Une synthèse sans ambiguité possible de l'amino-5 méthyl-1 nitro-4 pyrazole à partir de l'amino-5 méthyl-1 pyrazole, prouve que les attributions doivent être interchangées; les structures des composés qui dérivent de ces aminonitropyrazoles ont été corrigées en conséquence.

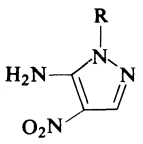
Canadian Journal of Chemistry, **49**, 3566 (1971)

Introduction

In earlier papers (1, 2) we have pointed out that simple Huckel molecular-orbital (H.m.o.) π-electron densities at amino nitrogen are linearly related to the chemical shifts of amino protons for aromatic amines in hydrogen-bond-acceptor solvents. We suggested also that these computationally trivial calculations could be used to predict chemical shifts.

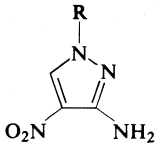
The present note reports an example of such prediction, resulting in the proposed interchange of the structures assigned to 5-amino-1-methyl-4-nitropyrazole (**1**) and to 3-amino-1-methyl-4-nitropyrazole (**2***a*) by Brown and co-workers (3).

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTSA LIBRARIES on 06/25/13
For personal use only.



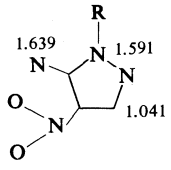
1

R = Me



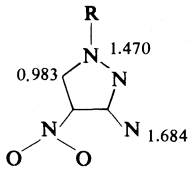
2

a R = Me
b R = H



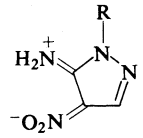
4

R = Me



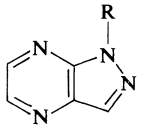
5

R = Me



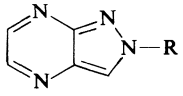
3

R = Me



6

a R = Me
b R = H



7

R = Me

and confirmation of the proposal by unambiguous synthesis of compound **1**.

Discussion and Results

Brown's group discovered that 4-methoxy-5-nitropyrimidine was converted into 3-amino-4-nitropyrazole (**2***b*) by hydrazine, and they obtained two products of respective m.p. 200 and 265–266° when the pyrimidine was treated with an excess of ethanolic methylhydrazine. The p.m.r. spectra of these products in dimethylsulfoxide-d_6 showed amino proton signals at δ 7.17 and 7.49, and they were assigned structures **1** and **2***a* respectively. However, simple resonance concepts suggest that the electron density at the 5-amino nitrogen in **1** should be significantly less than in **2***a*, in view of contributions from the form **3** (the charge displacement corresponding to **3** explains the extreme downfield position of the amino proton signal in *ortho*-nitroaniline (1)); no similar contribution is possible for structure **2***a*. Thus, qualitative considerations would indicate that **1** should have the lowfield amino proton signal at δ 7.49, and **2***a* the higher field signal at 7.17. This qualitative indication is confirmed by H.m.o. calculations on models of **1** and **2***a*, with results illustrated as **4** and **5**. The difference between the high and low field signals and the low and high charge densities indicates a response to electron density variations of *ca.* 7 p.p.m./electron, in agreement with previous work (1, 2). Further, the methyl proton signals of the compounds of m.p. 200 and 265–266° are at δ 3.65 and 3.57, and the pyrazole ring proton signals are at δ 8.42 and 7.82, respectively. If the compound of m.p. 265–266° is reassigned as **1**, and the compound of m.p. 200° as **2***a*, then the orders of the appropriate pairs of chemical shifts are in agreement with all previous charge-density/chemical shift correlations (4–7). The chemical shift patterns of the reassigned products are also consistent with the proton chemical shifts of the closely related isomeric amino-1-methyl-pyrazole-4-carbonitriles, whose structures are firmly established (8, 9). The shifts are compared in Table 1. Final confirmation of the validity of this interchange is afforded by nitration of 5-amino-1-methylpyrazole, which forms 5-amino-1-methyl-4-nitropyrazole, m.p. 266° (p.m.r. spectrum in dimethylsulfoxide-d_6: δ 3.60 (s, 3H (1-Me)); 7.60 (s, br, 2H (5-NH_2)); 7.87 (s, 1H (3-H)). Similar nitration of 5-amino-1-phenylpyrazole also afforded the 4-nitration product, 5-amino-4-nitro-1-phenylpyrazole, m.p. 154–156°, whose p.m.r. spectrum in hexadeuterodimethyl sulfoxide resembled that of **1**: δ 7.30 (s, br, 2H (5-NH_2)); 7.75 (s, 5H (1-Ph)); 8.20 (s, 1H (3-H)). The upfield shift of the amino signal as compared with **1** reflects ring-current shielding by the 1-phenyl substituent.

In view of the exchange of structural assignments for the amino-1-methyl-4-nitropyrazoles, assignments of structure for compounds derived from these species should be revised appropriately. For example, the compound described (3) as 4,5-diamino-1-methylpyrazole is actually 3,4-diamino-1-methylpyrazole, and the compound described as 1-methylpyrazolo(3,4-*b*)pyrazine (**6***a*) is the 2-methyl isomer **7**. This corrects a discrepancy between the coupling constants J_{56} for

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTSA LIBRARIES on 06/25/13
For personal use only.

TABLE 1. Proton chemical shifts for aminopyrazoles*

Literature structure	Correct structure	Proton shifts 1-Me	3-H	5-H	Amino
3-Amino-1-methyl-4-nitropyrazole (m.p. 265–266°)	5-Amino-1-methyl-4-nitropyrazole	3.57	7.82	—	7.49
	5-Amino-1-methylpyrazole-4-carbonitrile	3.57	7.57	—	6.57
5-Amino-1-methyl-4-nitropyrazole (m.p. 200°)	3-Amino-1-methyl-4-nitropyrazole	3.65	—	8.42	7.17
	3-Amino-1-methylpyrazole-4-carbonitrile	3.60	—	8.00	5.53

*In p.p.m from TMS, in dimethyl sulfoxide-d_6. Values for the aminonitro compounds from ref. 3.

1*H*-pyrazolo(3,4-*b*)pyrazine (**6***b*) and for the supposed **6***a* (the respective values are 3.0 and 1.8 Hz). With the revised assignment, the smaller coupling in the quinonoid ring of **7** is consistent with expectation from established bond order/coupling constant relationships (10, 11).

Finally, other structural revisions required include: 2,5,6- for 1,5,6-trimethylpyrazolo(3,4-*b*)pyrazine; 11- for 10-methyldibenzo(*f*,*h*)pyrazolo(3,4-*b*)quinoxaline; 3- for 5-diacetylamido-1-methyl-4-nitropyrazole; 3- for 5-acetamido-1-methyl-4-nitropyrazole; and 3- for 5-acetamido-4-amino-1-methylpyrazole.

Experimental

General

The p.m.r. measurements were made using a Varian A-60D spectrometer. Combustion analyses were carried out by Mrs. M. Petranovic of this laboratory using a Hewlett–Packard Model 185 CHN Analyzer. The H.m.o. calculations were made using a standard program (1), and with the following heteroatom parameters: pyrrole and nitro nitrogen, and oxygen, $h = +1$; pyridine and amino nitrogen, $h = +\frac{1}{2}$.

Reference Samples and Starting Materials

3-Amino-1-methylpyrazole-4-carbonitrile, m.p. 135–136°, was prepared using the method of Schmidt and co-workers (8); 5-amino-1-methylpyrazole-4-carbonitrile, m.p. 224–225°, was prepared following Cheng and Robins' method (9). 5-Amino-1-phenylpyrazole was a commercial sample (Aldrich Chemical Company) and was used without further purification.

5-Amino-1-methylpyrazole

5-Amino-1-methylpyrazole-4-carbonitrile (30 g) was dissolved cautiously in 85% w/w aqueous sulfuric acid (100 ml) and heated under reflux for 12 h. The mixture was cooled and added to crushed ice (500 g), basified with aqueous ammonia, and left overnight at 5°. The mixture was filtered and the filtrate extracted five times with 200 ml portions of chloroform. The chloroform extract was dried ($MgSO_4$) and the solvent was removed under reduced pressure, yielding 5-amino-1-methylpyrazole (19.9 g, 84%), m.p. 69° (lit. (12) m.p. 71–72°); p.m.r. spectrum in dimethylsulfoxide-d_6: δ 3.52 (s, 3H (1-Me)); 5.00 (s, br, 2H (5-NH_2)); 5.27 (d, $J = 2$ Hz, 1H (4-H)); 7.00 (d, $J = 2$ Hz, 1H (3-H)).

5-Amino-1-methyl-4-nitropyrazole

5-Amino-1-methylpyrazole (5.00 g) was dissolved in ice-cold 36 *N* sulfuric acid (10 ml) and 70% nitric acid (5 ml) and allowed to stand for 3 h. The reaction mixture was basified with aqueous ammonia and extracted with chloroform (200 ml) followed by ethyl acetate (5 × 100 ml). Evaporation of the ethyl acetate followed by crystallization from methanol yielded 5-amino-1-methyl-4-nitropyrazole (1.6 g, 23%), m.p. 266°.

Anal. Calcd. for $C_4H_6N_4O_2$: C, 33.81; H, 4.26; N, 39.42. Found: C, 33.80; H, 4.17; N, 39.30.

5-Amino-4-nitro-1-phenylpyrazole

5-Amino-1-phenylpyrazole (1.00 g) was dissolved in acetic anhydride (10 ml) and the solution was cooled to 0°. To the cold, stirred solution was added 90% nitric acid (2 ml); the temperature was maintained between −5 and 0° by addition of dry ice. After addition of the acid was complete, the reaction mixture was stirred for a further 5 min, and was added with stirring to crushed ice (100 g). The precipitate was collected and crystallized from ethanol, yielding 5-amino-4-nitro-1-phenylpyrazole (1.20 g, 92%), m.p. 154–156°.

Anal. Calcd. for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 53.10; H, 3.79; N, 26.90.

This research was supported by the National Cancer Institute of Canada and the National Research Council of Canada. We acknowledge Dr. D. J. Brown's courtesy in discussion of our results.

1. B. M. LYNCH, B. C. MACDONALD, and J. G. K. WEBB. Tetrahedron, **24**, 3595 (1968).
2. B. M. LYNCH. Tetrahedron Lett. 1357 (1969).
3. M. E. C. BIFFIN, D. J. BROWN, and Q. N. PORTER. J. Chem. Soc. C, 2159 (1968).
4. G. FRAENKEL, R. E. CARTER, and A. MCLACHLAN. J. Am. Chem. Soc. **82**, 5846 (1960).
5. T. SCHAEFER and W. G. SCHNEIDER. Can. J. Chem. **41**, 966 (1963).
6. B. M. LYNCH and H. J. M. DOU. Tetrahedron Lett. 2627 (1966).

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTSA LIBRARIES on 06/25/13
For personal use only.

7. B. M. LYNCH, A. J. ROBERTSON, and J. G. K. WEBB. Can. J. Chem. **47**, 1129 (1969).
8. P. SCHMIDT, K. EICHENBERGER, M. WILHELM, and J. DRUEY. Helv. Chim. Acta, **42**, 743 (1959).
9. C. C. CHENG and R. K. ROBINS. J. Org. Chem. **21**, 1240 (1956).
10. N. JONATHAN, S. GORDON, and B. P. DAILEY. J. Chem. Phys. **36**, 2443 (1962).
11. W. B. SMITH, W. H. WATSON, and S. CHIRANJEEVI. J. Am. Chem. Soc. **89**, 1438 (1967).
12. H. DORN, G. HILGETAG, and A. ZUBEK. Angew. Chem. **76**, 920 (1964).

Isomerization of 1-*exo*-4,5,6,7,8,8-Heptachloro-2,3-*endo*-epoxy-3*a*,4,7,7*a*-tetrahydro-4,7-methanoindane with Base

W. P. COCHRANE AND M. A. FORBES[1]

Analytical Services Section, Plant Products Division, Canada Department of Agriculture, Ottawa, Canada

Received June 8, 1971

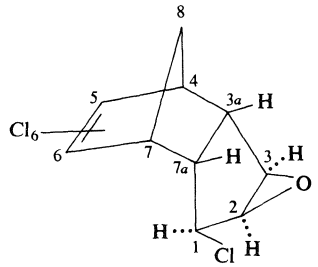
Treatment of the title compound, **2**, with excess sodium methoxide produced an unsaturated secondary alcohol, **3**. Structure elucidation was achieved by MnO_2 oxidation followed by $CrCl_2$ reductive dechlorination to give as the major product 2-oxa-4,5,6,7,8,8-hexachloro-3*a*,4,7,7*a*-tetrahydro-4,7-methanoindane.

Le composé, **2**, donné dans le titre, traité avec un excès de méthylate de sodium a conduit à un alcool secondaire insaturé **3**. La recherche de la structure a été menée à bien par une oxydation avec MnO_2 suivie d'une déchloration réductive par $CrCl_2$ pour donner comme produit principal l'oxa-2 hexachloro-4,5,6,7,8,8-tétrahydro-3*a*,4,7,7*a* méthano-4,7 indane.

Canadian Journal of Chemistry, **49**, 3569 (1971)

In connection with previous work on polychlorinated cyclodiene pesticides it was observed that the action of base on the biological metabolite of heptachlor,[2] namely heptachlor epoxide **1**, resulted in preferential epoxide isomerization, yielding an α,β-unsaturated alcohol (1). Molecules containing the required configuration *i.e.*, a *trans* coplanar arrangement of one of the carbon–oxygen bonds of the epoxide ring and a hydrogen on an adjacent carbon, apparently undergo transformation readily (2). In heptachlor epoxide the *cis*-arrangement of the epoxy ring to the C-1 chlorine atom resulted in initial abstraction of the C-1 proton (1). As an extension to this work it was of interest to study the isomeric compound **2** in which the epoxy group is *trans* to the C-1 chlorine atom (3).

Accordingly, a solution of *trans*-epoxide **2** in methanol was treated under reflux with an excess of sodium methoxide. Reaction occurred readily to yield, after water–hexane partition, an oil which was purified by distillation, b.p. 130–132°/0.1 mm. The molecular formula $C_{10}H_5Cl_7O$ was established by elemental analysis and mass spectrometry. The i.r. spectrum indicated a bonded hydroxyl, 3380 cm^{-1} together with a double bond at 1595 cm^{-1}. Previously, an isomeric hydroxyl-containing product had been formed from the *cis*-epoxide **1**. The n.m.r. spectrum substantiated the presence of only one olefinic proton and one hydroxyl proton whose signals appeared at τ 3.95 and 7.21 respectively. Consideration of the foregoing data and the



1

[1]Present address: Inland Waters Branch, Department of Energy, Mines and Resources, Federal Building, Moncton, New Brunswick.

[2]Heptachlor is the common name for the insecticidal compound 1-*exo*-4,5,6,7,8,8-heptachloro-3*a*,4,7,7*a*-tetrahydro-4,7-methanoindene.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTSA LIBRARIES on 06/25/13
For personal use only.