

Ring opening of pyridines: the pseudo-*cis* and pseudo-*trans* isomers of tetra-*n*-butylammonium 4-nitro-5-oxo-2-pentenenitrilate

Matthias Zeller,^a Virginia B. Pett^b and LeRoy W. Haynes^{b*}

^aDepartment of Chemistry, Youngstown State University, One University Plaza, Youngstown, OH 44555-3663, USA, and ^bDepartment of Chemistry, The College of Wooster, 943 College Mall, Wooster, OH 44691, USA
Correspondence e-mail: haynes@wooster.edu

Received 4 March 2007

Accepted 19 April 2007

Online 11 May 2007

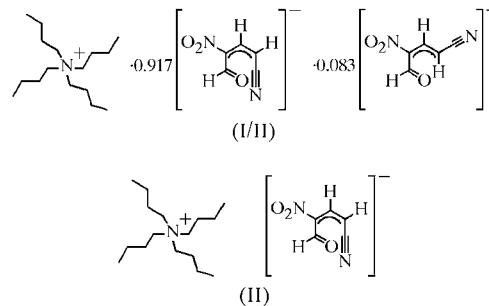
The reaction of 2-chloro-5-nitropyridine with two equivalents of base produces the title carbanion as an intermediate in a ring-opening/ring-closing reaction. The crystal structures of the tetra-*n*-butylammonium salts of the intermediates, $C_{16}H_{36}N^+ \cdot C_5H_3N_2O_3^-$, revealed that pseudo-*cis* and pseudo-*trans* isomers are possible. One crystal structure displayed a mixture of the two isomers with approximately 90% pseudo-*cis* geometry and confirms the structure predicted by the S_N (ANRORC) mechanism. The pseudo-*cis* intermediate undergoes a slow isomerization over a period of months to the pseudo-*trans* isomer, which does not have the appropriate geometry for the subsequent ring-closing reaction. The structure of the pure pseudo-*trans* isomer is also reported. In both isomers, the negative charge is highly delocalized, but relatively small differences in C—C bond distances indicate a system of conjugated double bonds with the nitro group bearing the negative charge. The packing of the two unit cells is very similar and largely determined by the interactions between the planar carbanion and the bulky tetrahedral cation.

Comment

During the 1980s, Reinheimer *et al.* (1980, 1984) investigated the reaction of 2-chloro-5-nitropyridine with an excess of sodium hydroxide in dimethyl sulfoxide/water solutions. Using visible spectroscopy, in addition to 1H and ^{13}C NMR, they were able to show that a relatively stable intermediate was formed. They proposed that the pseudo-*cis* isomer, (I), would enable the intermediate to undergo the second part of the reaction sequence, namely ring closure. This reaction sequence was named by van der Plas (1978) as the S_N (ANRORC) process (addition of the nucleophile, ring opening and ring closure).

If only two equivalents of hydroxide were used, the intermediate formed from 2-chloro-5-nitropyridine was reasonably

stable in the reaction medium. However, over a period of months we observed that the intermediate either slowly



isomerized or decomposed to formate. We followed these transformations using 1H NMR spectroscopy. In contrast, 2-chloro-3-nitropyridine in the presence of two equivalents of sodium hydroxide forms a pseudo-*cis* intermediate that, during work-up, readily isomerizes to a pseudo-*trans* intermediate, (III). The structures of both of the intermediates from 2-chloro-3-nitropyridine were determined using NMR spectroscopy and X-ray crystallography (Haynes & Pett, 2007).

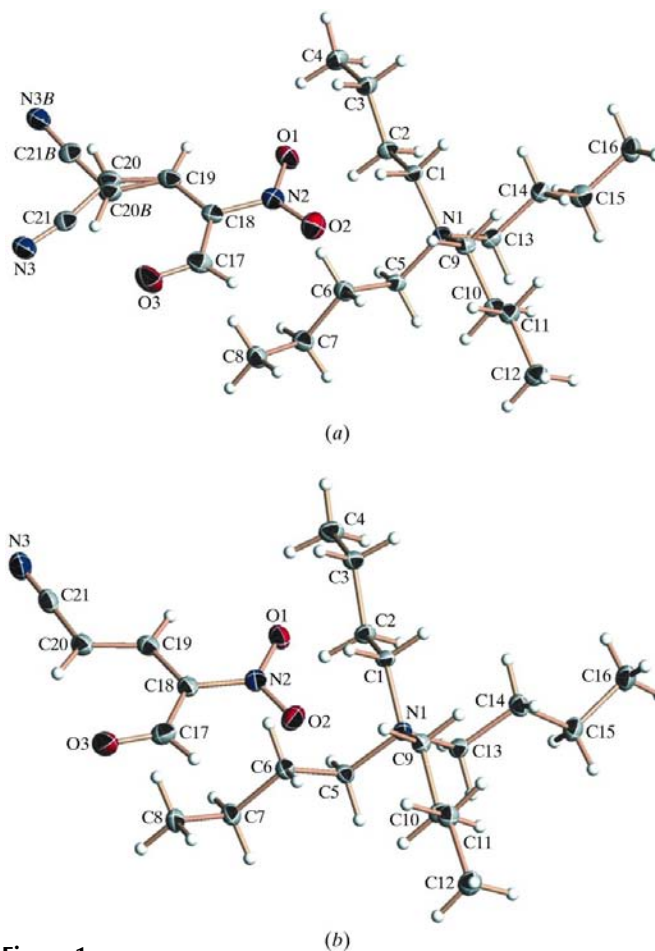
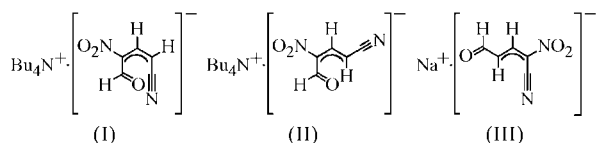


Figure 1
Displacement ellipsoid diagrams at the 50% probability level of the molecular structures of (a) the pseudo-*cis*/pseudo-*trans* mixture, (I/II), showing both components, *viz.* pseudo-*cis* intermediate (I) and pseudo-*trans* intermediate (II) (B labels), in the disordered structure, and (b) the pure pseudo-*trans* intermediate, (II).

The dramatic difference between the isomerization rates of intermediates from two very similar starting materials prompted us to continue our investigations with the intermediates from 2-chloro-5-nitropyridine. In order to verify our assumptions concerning the structures of the two intermediates, we conducted crystallization experiments with samples containing predominantly one isomer or the other, as indicated by the ^1H NMR spectra.



One sample (as the tetra-*n*-butylammonium salt) gave disordered monoclinic crystals that were found to consist of a mixture of mainly the pseudo-*cis* isomer, (I), with a small but significant amount of the pseudo-*trans* isomer, (II) (Fig. 1a). Several crystals from different crystallization attempts were analyzed, resulting in all cases in similar pseudo-*cis* to pseudo-*trans* ratios. For the data set used here, the ratio refined to 91.7 (3) to 8.3 (3)% in favor of the pseudo-*cis* isomer.

The X-ray crystallographic study using the crystals isolated from a sample that was stable in solution for eight months (again as the tetra-*n*-butylammonium salt) showed that these crystals were made up only of carbanions in the pseudo-*trans* geometry, (II) (Fig. 1b). This pure isomer also crystallized with the same monoclinic space group, $P2_1/n$, and with an almost

identical unit-cell volume. The two monoclinic cells have comparable unit-cell axes and β angles, but the positions of the glide planes differ. Thus, the designation of the unit cell axes is different; a , b and c in the (I/II) mixed crystal are converted into c , a and b in the crystal of pure (II).

The type of packing in the two different cells is very similar (Fig. 2), with layers of the planar carbanions alternating with the tetra-*n*-butylammonium cations. The orientation of the ions and their orientation with respect to each other is the same in both cells; only the separation between the ions varies slightly between the two structures. The largest difference is observed for the closest distance of the O atoms of adjacent nitro groups, which is 5.6827 (18) Å in (II) and 5.821 (3) Å in (I/II) [the symmetry operator relating the adjacent molecules is $(-x + 1, -y + 1, -z + 1)$].

Within the layers, the carbanions are arranged in loosely connected dimers. In both pseudo-*trans* (II) and disordered

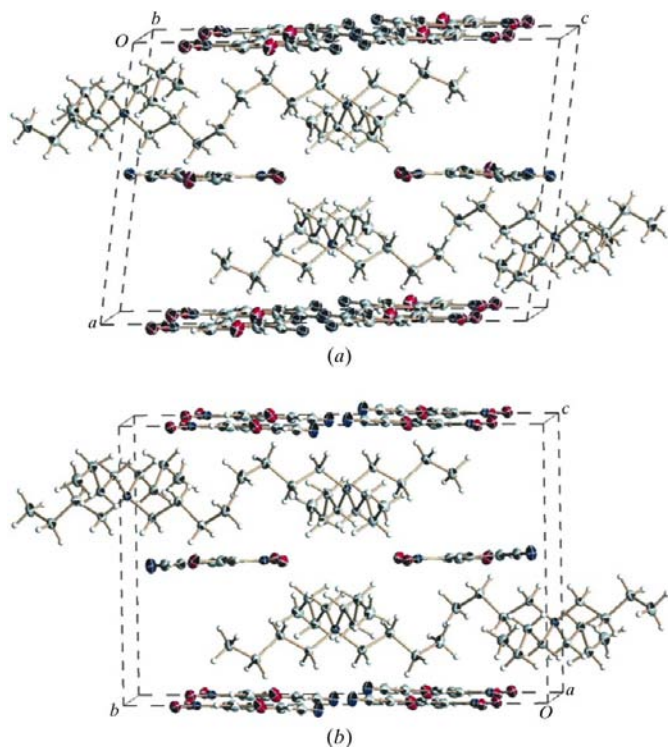


Figure 2
A packing view of the crystal structures, drawn with 50% probability displacement ellipsoids, showing the layered nature of the two structures, *viz.* (a) the disordered structure of the pseudo-*cis*/pseudo-*trans* mixture, (I/II), showing both components, and (b) the pure pseudo-*trans* intermediate, (II).

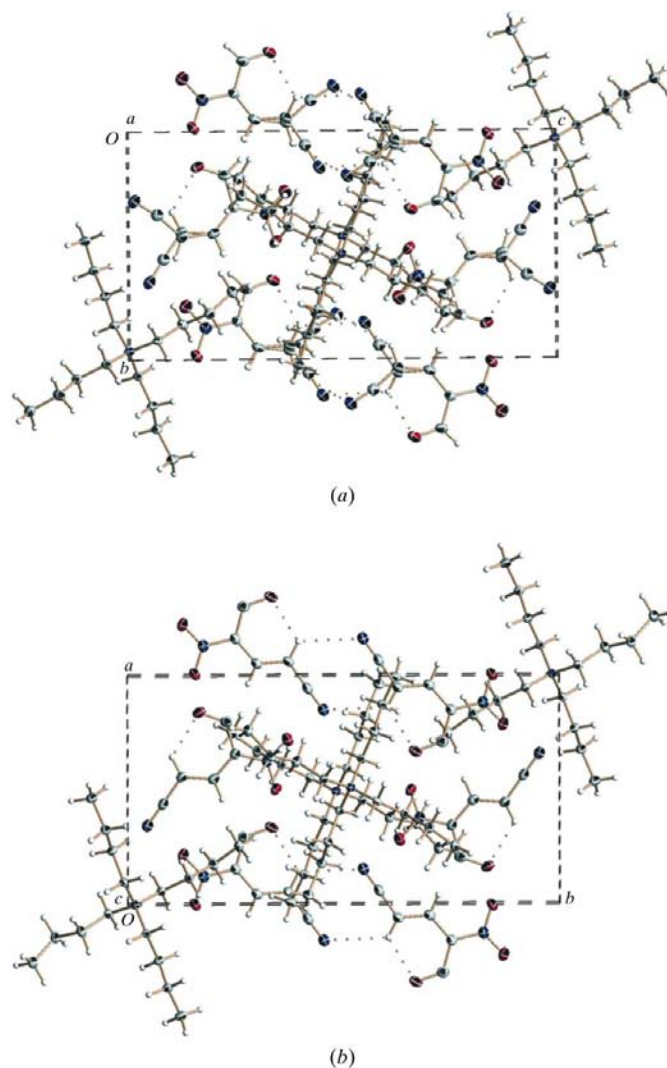


Figure 3
A packing view of the crystal structures of (a) the disordered structure of the mixture showing both the main pseudo-*cis* intermediate, (I), and the minor pseudo-*trans* intermediate, (II), and (b) the pure pseudo-*trans* intermediate, (II). Displacement ellipsoids are drawn at the 50% probability level.

(I/II), the nitrile groups are arranged in such a way that the N atom interacts with atom H20 of the neighboring anion to form a very weak intermolecular hydrogen bond (Fig. 3). For the pseudo-*cis* isomer, (I), the interaction is slightly weaker, with a C20...N3 distance of 3.519 (4) Å. For the pseudo-*trans* geometry, in both types of crystals, the hydrogen bond is slightly strengthened, and the C...N distances are 3.39 (4) and 3.348 (2) Å in the structures of (I/II) and (II), respectively. (See Tables 1 and 2 for the hydrogen-bonding parameters.) However, even this slightly shorter hydrogen bond is not unusually strong. A search of the Cambridge Structural Database for nitrile dimers connected *via* similar hydrogen bonds revealed 58 compounds with both hydrogen bonds equal to or shorter than 2.8 Å (Version 5.27; Allen, 2002).

In the pseudo-*trans* geometry, atom H20 also forms an intramolecular hydrogen bond with aldehyde atom O3, thus possibly stabilizing the pseudo-*trans* geometry slightly as compared with the pseudo-*cis* isomer (Tables 1 and 2, and Fig. 3). Nevertheless, all the hydrogen-bonding interactions seem to be rather weak and are probably not a significant directing force towards the overall packing mode. It seems more likely that the packing is determined by the electrostatic interactions between the alternating layers of carbanions and tetra-*n*-butylammonium cations.

The C—C bonds in carbanions (I), (II) and (III) are shorter than standard single bonds, indicating considerable delocalization of the negative charge over each anion (Table 3). However, the C19—C20 distances in all three anions are significantly shorter than the other C—C bonds and almost as short as a standard double bond. Also, the C18—N2 distances in the nitro group are shorter than a single C—N bond, while the N2—O1 and N2—O2 distances are longer than an N=O double bond. The bond distances in these three carbanions exhibit a conjugated system of double bonds, revealing that the electron distribution is clearly directed by the nitro group, the most powerful electron-withdrawing substituent in the anions. Thus, the structures coincide with what we would expect from the electronegativities of the atoms.

Experimental

The original samples of the intermediates as their sodium salts were prepared following the directions of Reinheimer *et al.* (1980, 1984). Because of what appeared to be oxidation of the intermediate, one reaction of 2-chloro-5-nitropyridine with sodium hydroxide was carried out under a nitrogen atmosphere. Interestingly, the intermediate formed was (II). That reaction provided the sample of (II) that was used for the crystal structure determination. To produce crystalline material suitable for the vapor diffusion process, tetra-*n*-butylammonium bromide was added to an aqueous or water/dimethyl sulfoxide solution of the sodium salt. After freeze-drying to remove solvent(s), the tetra-*n*-butylammonium salt of the intermediate was separated from inorganic salts by extraction with acetone. Evaporation of the acetone gave a solid suitable for crystallization. ¹H NMR: pseudo-*cis* (I) (D₂O/D₆DMSO): δ 9.75, 6.97, 5.23; pseudo-*trans* (II) (D₂O/D₆DMSO): δ 9.80, 7.37, 6.20. Suitable crystals of the tetra-*n*-butylammonium salts of the mixture of both intermediates were grown by vapor diffusion of hexanes into dichloromethane solutions of the intermediates.

Compound (I/II)

Crystal data

C ₁₆ H ₃₆ N ⁺ ·C ₅ H ₃ N ₂ O ₃ [−]	V = 2189.0 (5) Å ³
M _r = 381.55	Z = 4
Monoclinic, P2 ₁ /n	Mo Kα radiation
a = 12.2793 (16) Å	μ = 0.08 mm ^{−1}
b = 9.7588 (12) Å	T = 100 (2) K
c = 18.422 (2) Å	0.6 × 0.4 × 0.25 mm
β = 97.444 (2)°	

Data collection

Bruker SMART APEX CCD diffractometer	21198 measured reflections
Absorption correction: multi-scan (SADABS in SAINT-Plus; Bruker, 2003)	5406 independent reflections
T _{min} = 0.848, T _{max} = 0.981	4323 reflections with I > 2σ(I)
	R _{int} = 0.047

Refinement

R[F ² > 2σ(F ²)] = 0.069	3 restraints
wR(F ²) = 0.175	H-atom parameters constrained
S = 1.13	Δρ _{max} = 0.46 e Å ^{−3}
5406 reflections	Δρ _{min} = −0.22 e Å ^{−3}
258 parameters	

Table 1

Hydrogen-bond and short-contact geometry (Å, °) for (I/II).

D—H...A	D—H	H...A	D...A	D—H...A
C20—H20...N3 ⁱ	0.95	2.75	3.519 (4)	139
C20B—H20B...N3B ⁱ	0.95	2.87	3.39 (4)	116
C20B—H20B...O3	0.95	2.25	2.86 (4)	122

Symmetry code: (i) −x + 1, −y + 1, −z + 2.

Pure (II)

Crystal data

C ₁₆ H ₃₆ N ⁺ ·C ₅ H ₃ N ₂ O ₃ [−]	V = 2190.2 (3) Å ³
M _r = 381.55	Z = 4
Monoclinic, P2 ₁ /n	Mo Kα radiation
a = 9.7894 (9) Å	μ = 0.08 mm ^{−1}
b = 18.3872 (16) Å	T = 100 (2) K
c = 12.2327 (11) Å	0.73 × 0.59 × 0.10 mm
β = 95.894 (2)°	

Data collection

Bruker SMART APEX CCD diffractometer	18699 measured reflections
Absorption correction: multi-scan (SADABS in SAINT-Plus; Bruker, 2003)	5402 independent reflections
T _{min} = 0.792, T _{max} = 0.992	4809 reflections with I > 2σ(I)
	R _{int} = 0.033

Refinement

R[F ² > 2σ(F ²)] = 0.058	248 parameters
wR(F ²) = 0.136	H-atom parameters constrained
S = 1.19	Δρ _{max} = 0.40 e Å ^{−3}
5402 reflections	Δρ _{min} = −0.18 e Å ^{−3}

Table 2

Hydrogen-bond and short-contact geometry (Å, °) for (II).

D—H...A	D—H	H...A	D...A	D—H...A
C20—H20...N3 ⁱ	0.95	2.78	3.348 (2)	119
C20—H20...O3	0.95	2.26	2.887 (2)	123

Symmetry code: (i) −x + 1, −y + 2, −z + 1.

Table 3

A comparison of selected bond lengths (Å) in (I), (II) and (III).

Compound	(I) ^a	(II) ^b	(II) ^c	(III) ^d
O3—C17	1.225 (3)	1.233 (2)	1.225 (3)	1.249 (3)
C17—C18	1.429 (3)	1.428 (2)	1.429 (3)	1.421 (3)
C18—C19	1.427 (3)	1.428 (2)	1.427 (3)	1.361 (3)
C19—C20	1.353 (4)	1.354 (2)	1.353 (4)	1.408 (3)
C20—C21	1.428 (4)	1.424 (2)	1.44 (2)	1.418 (3)
C18—N2	1.403 (3)	1.400 (2)	1.403 (3)	1.378 (3)
C21—N3	1.143 (3)	1.153 (2)	1.163 (18)	1.150 (3)
N2—O1	1.263 (3)	1.2602 (18)	1.263 (3)	1.246 (2)
N2—O2	1.253 (3)	1.2586 (18)	1.253 (3)	1.264 (3)

Notes: (a) this work, pseudo-*cis* isomer, cocrystallized sample (I/II); (b) this work, pure pseudo-*trans* sample (II); (c) this work, pseudo-*trans* isomer, cocrystallized sample (I/II); (d) Haynes & Pett (2007), (III); the same atom numbering as in samples (I/II) and (II) is used here for consistency.

The crystals grown from the original sample exhibit a disorder of the major pseudo-*cis* intermediate, (I), with a minor presence of the pseudo-*trans* isomer, (II). The data of several crystals were collected (only the best data set is reported here) and all structures exhibited similar pseudo-*cis* to pseudo-*trans* ratios [0.917 (3) to 0.083 (3) for the reported example]. The bond distances within the minor component were restrained to be the same as those of the major component (within a standard deviation of 0.02 Å), and the anisotropic displacement parameters of the minor component atoms were set to be the same as those of the major isomer. Atom C19, which by itself is not disordered, was included in the disorder, but the major and minor component atoms were set to have the same coordinates and anisotropic displacement parameters, thus allowing us to add H19 and H19B in calculated positions rather than refining their positions using constraints. In both structures, all H atoms were placed in calculated positions, with C—H distances of 0.98, 0.99 and 0.95 Å for methyl, methylene and alkene H atoms, respectively, and were refined with isotropic displacement parameters of 1.5 (methyl) or 1.2 (methylene,

alkene) times U_{eq} of the adjacent C atom. Methyl H atoms were allowed to rotate to best fit the experimental electron density.

For both determinations, data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT-Plus* (Bruker, 2003); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

This report is dedicated to the memory of John D. Reinheimer who was accidentally killed in December 2003 when struck by a vehicle near his home. MZ was supported by NSF grant No. 0111511. The diffractometer was funded by NSF grant No. 0087210, by Ohio Board of Regents grant No. CAP-491 and by YSU.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3045). Services for accessing these data are described at the back of the journal.

References

- Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.
 Bruker (1997). *SMART for WNT/2000*. Version 5.630. Bruker AXS Inc., Madison, Wisconsin, USA.
 Bruker (2000). *SHELXTL*. Version 6.14. Bruker AXS Inc., Madison Wisconsin, USA.
 Bruker (2003). *SAINT-Plus*. Version 6.45. Bruker AXS Inc., Madison, Wisconsin, USA.
 Haynes, L. W. & Pett, V. B. (2007). *J. Org. Chem.* **72**, 633–635.
 Plas, H. C. van der (1978). *Acc. Chem. Res.* **11**, 462–468.
 Reinheimer, J. D., Mayle, L. L., Dolnikowski, G. G. & Gerig, J. T. (1980). *J. Org. Chem.* **45**, 3097–3100.
 Reinheimer, J. D., Sourbatis, N., Lavallee, R. L., Goodwin, D. & Gould, G. L. (1984). *Can. J. Chem.* **62**, 1120–1123.