A new redox-denitration reaction of aromatic nitro compounds

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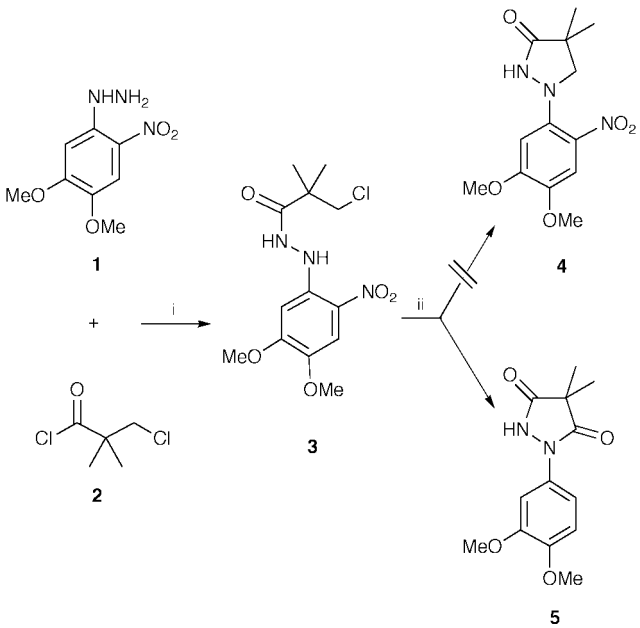
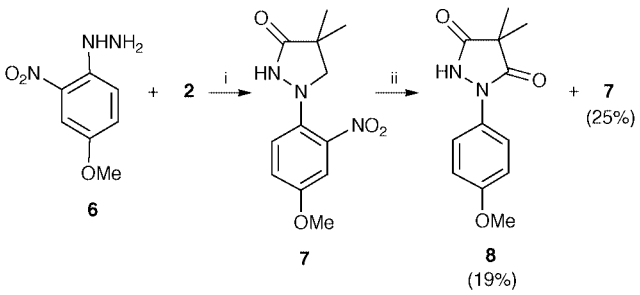
When 4,4-dimethyl-1-(2-nitrophenyl)pyrazolidin-3-one 9 is heated in pyridine containing pyridine hydrochloride it is transformed into 4,4-dimethyl-1-phenylpyrazolidin-3,5-dione 10 in which the methylene group has been oxidised and the nitro group has disappeared; two further examples of the same reaction, of pyrazolidinones 4 and 7, are reported together with a mechanistic rationalisation of this curious reaction.

New reactions of aromatic nitro groups are rare. We recently discovered one during an unsuccessful attempt to synthesise the 1-arylpyrazolidin-3-one **4** from 4,5-dimethoxy-2-nitrophenylhydrazine **1** and 3-chloropivaloyl chloride **2**. After an initial reaction in cold pyridine which gave **3**,† mp 163 °C (isolable in 90% yield), the reaction mixture was heated under reflux for 24 h. From this complex reaction we could not isolate any **4**, but only a rather low yield of the 1-arylpyrazolidin-3,5-dione **5**,† mp 189–191 °C (23%), in which the nitro group has been replaced by hydrogen and the pyrazolidinone methylene group oxidised to a carbonyl group (Scheme 1). Compound **5** was synthesised independently from 3,4-dimethoxyphenylhydrazine and dimethylmalonyl dichloride. We assume that **1** and **2** are converted *via* **3** into the desired pyrazolidinone **4**, but this has reacted further to give **5**. On heating preformed **3** in pyridine for 20 h, **5** was again formed as the major product. This unexpected conversion of **4** into **5** is a novel redox reaction in which the nitro group has presumably oxidised the adjacent methylene group and has undergone, most unusually, complete cleavage from the aromatic ring with overall loss of the elements of nitroxyl, HNO.



Scheme 1 *Reagents and conditions*: i, pyridine, 5 °C, N_2, 1 h; ii, pyridine, 115 °C, N_2, 24 h.

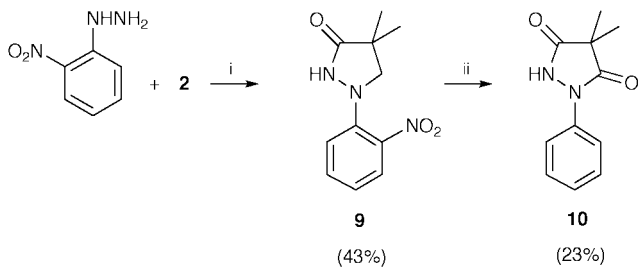


Scheme 2 *Reagents and conditions*: i, pyridine, 5 °C, N_2, 1 h, then room temp., 1 h, then 115 °C, 2 h, ii; pyridine 115 °C, N_2, 20 h.

We performed the same reaction (Scheme 2) with the monomethoxyphenylhydrazine **6** and acid chloride **2** in cold pyridine, to give the acylic hydrazide intermediate (TLC), followed by brief heating (2 h) to give the expected 1-arylpyrazolidin-3-one **7** as the major product. After extended heating (20 h) a mixture of **7** (25%) and the denitrated pyrazolidin-3,5-dione **8** (19%) was isolated. The formation of the monomethoxy product **8** is distinctly slower than for the dimethoxy product **5**.

Finally we treated 2-nitrophenylhydrazine with acid chloride **2** in cold pyridine and then at 90 °C for 11 h to give the nitrophenylpyrazolidin-3-one **9**,† mp 196–198 °C (43%) (Scheme 3). When pure compound **9** was heated in pyridine for up to 5 days there was very little reaction,‡ but when heated in pyridine containing pyridine hydrochloride (1 equiv.) to simulate the conditions of the reactions of **1** and **6**, the overall loss of HNO again occurred to give 1-phenylpyrazolidin-3,5-dione **10** (mp 180 °C, lit.[1] 180–182 °C) (23%) after 20 h. Product **10** was also synthesised from phenylhydrazine and dimethylmalonyl dichloride.

This new acid-catalysed redox-denitration reaction could thus be general for the conversion of 1-(2-nitroaryl)pyrazolidin-3-ones, like **4**, **7** and **9**, into 1-arylpyrazolidin-3,5-diones, like **5**, **8** and **10**. A possible mechanism is outlined in Scheme 4, for the simplest case. Aromatic nitro groups are well known to interact in thermal, photolytic and catalysed reactions with a range of *ortho* substituents,[2] often being reduced to nitroso, azo, azoxy or amino groups, but very rarely with concomitant cleavage of the aryl–nitrogen bond.[3] Since the methylene group would be activated towards oxidation by the adjacent pyrazolidinone



Scheme 3 *Reagents and conditions*: i, pyridine, 50 °C, N_2, 1 h, then 90 °C, 11 h; ii, pyridine, py·HCl (1 equiv.), 115 °C, N_2, 20 h.

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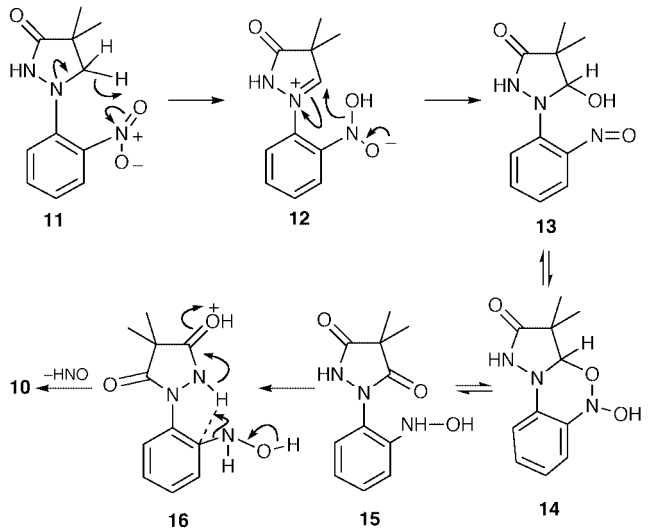

Scheme 4

nitrogen atom, it seems likely that the first step would be an intramolecular hydride transfer to the nitro group (arrows in **11**). This is exactly analogous to that proposed for tertiary amines, when the amine replaces our heterocyclic ring (the *tert*-amino effect).[4] This would give the iminium ion **12** which could collapse to the nitroso compound **13** or its tricyclic tautomer **14**; **13** and **14** would be in equilibrium with each other and with the hydroxylamine **15**.

The final and most unusual step would then be the loss of nitroxyl, HNO,[5] from **15** to give the isolated product **10**; this outcome may depend critically upon the particular structural features of the starting pyrazolidinones. Since protonation at the benzene 2-position must presumably be involved, the reaction should be acid-catalysed (as observed), inter- or intra-molecularly. It could occur, for example, in the conjugate acid **16** of **15** as shown (arrows in **16**). In this mechanism (Scheme 4) various steps would be facilitated by the electron releasing groups in the mono- and di-methoxy compounds, in accord with the observed relative rates of reaction. Further work is required to establish the scope and mechanism of this new reaction.

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Notes and references

† The structures of all new compounds are based upon IR, MS, LCMS, HRMS and ^{1}H NMR spectroscopy.

‡ Some intractable material containing traces of **10** (mass spectrometry) was formed.

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