Oxidative nucleophilic substitution of hydrogen in nitrobenzene with 2-phenylpropionitrile carbanion and potassium permanganate oxidant

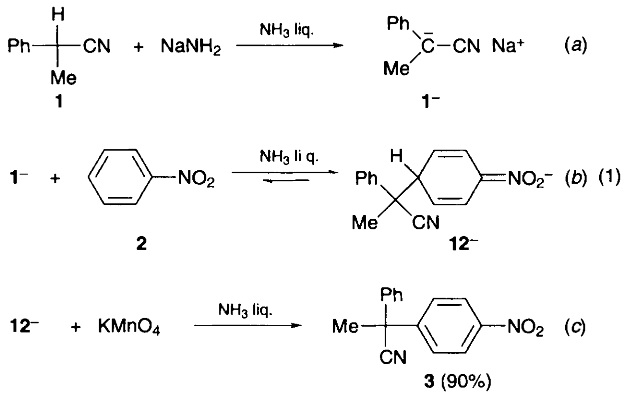
Mieczysław Mąkosza,* Krzysztof Staliński and Cezary Klępka

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, PL 01-224 Warsaw, Poland

The carbanion of 2-phenylpropionitrile adds to nitrobenzene in the *p*-position in liquid ammonia to give the relative stable σ^H-adduct which is oxidised with $KMnO_4$ to 2-phenyl-2-(4-nitrophenyl)propionitrile; the relationships of rates of various reactions in these systems are estimated.

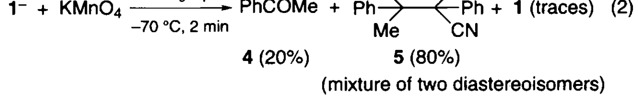
Nucleophilic substitution of hydrogen in aromatic systems has recently been recognized as a general process.[1] It can occur *via* numerous mechanisms and pathways, the most general of them appears to be Vicarious Nucleophilic Substitution VNS, which occurs in the reaction of nucleophiles containing leaving groups X with electrophilic arenes and proceeds *via* the formation of the corresponding σ^H-adducts followed with base induced β-elimination of HX.[2] Oxidation of the σ^H-adducts, which is an obvious way to remove the hydride anions resulting in the formation of the substitution products suffers from a few limitations, the main one being the sensitivity of nucleophiles towards oxidation. Thus in the frequent cases of unfavourable addition equilibrium oxidation of the nucleophiles becomes the main process. Oxidative nucleophilic substitution of hydrogen (ONSH) proceeds satisfactorily when Nu^- are resistant towards oxidation and when the equilibrium of the addition assures high concentrations of σ^H-adducts and low concentrations of Nu^- *etc.*[3] One could also expect that there should be the possibility of finding an oxidant which oxidizes σ^H-adducts faster than the starting nucelophilic agents in spite of high general sensitivity of the latter towards oxidation. A guiding line in this respect could be the electrostatic repulsion between anionic oxidants and anionic nucleophiles, in that such repulsion should be much weaker for σ^H-adducts where the negative charge is substantially delocalized.

It has been known for many years that $KMnO_4$ in liquid ammonia is an excellent oxidant for σ^H-adducts formed by ammonia or amide nucleophiles and highly electrophilic arenes, particularly heteroarenes. This oxidative variant of the Chichibabin amination is currently of great practical use.[4] We have therefore attempted to use these conditions for ONSH in nitroarenes with carbanions expecting that the latter, although readily oxidised with oxygen, should be more resistant towards oxidation with MnO_4^- anions due to electrostatic repulsion.



When a mixture of the carbanion of 2-phenylpropionitrile 1^- generated from **1** and sodium amide in liquid ammonia and nitrobenzene **2** was treated with $KMnO_4$, the product of ONSH, 2-(4-nitrophenyl)-2-phenylpropionitrile **3**, was produced in high yield.

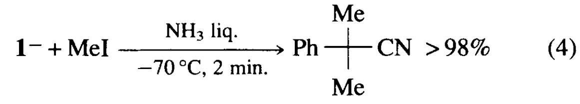
Although it was reported that 1^- reacts with nitroarenes without $KMnO_4$,[5] under the conditions used here there is negligible conversion of 1^- and **2** into **3** or other products. This result generates a few questions which should be answered.†,‡. i, How resistant are carbanions of **1** towards $KMnO_4$?



Oxidation of the carbanions 1^- with potassium permanganate is a fast reaction. ii, What is the relationship between the rates of oxidation of the carbanion and its addition to nitrobenzene?

$$1^- + [2 + KMnO_4] \xrightarrow[-70\,°C,\ 2\ min.]{NH_3\ liq.} 3\ (10\%) + 4\ (18\%) + 5\ (65\%) \qquad (3)$$

When a solution of the carbanion was added to an equimolar mixture of **2** and $KMnO_4$ the main process was the oxidation of the carbanion and not of the σ^H-adduct 12^-. Thus the oxidation of 1^- proceeds faster than its addition to **2**. From the results of eqns. (1) and (3) it appears that the equilibrium (1*b*) is shifted to the right. iii, Is equilibrium (1*b*) really shifted to the right as indicated by the results of eqns. (1), (2) and (3)? In order to confirm this supposition and estimate the position of the equilibrium the methylation of 1^- with MeI was studied.



$$1^- + MeI \xrightarrow[-70\,°C,\ 2\ min.]{NH_3\ liq.} Ph-\overset{Me}{\underset{Me}{C}}-CN\ >98\% \qquad (4)$$

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$$MeI + [1^- + 2] \xrightarrow[-70\,°C,\ 2\ min.]{NH_3\ liq.} 6\ (20\%) + 1\ (80\%) \qquad (5)$$

$$1^- + [2 + MeI] \xrightarrow[-70\,°C,\ 2\ min.]{NH_3\ liq.} 6\ (52\%) + 1\ (48\%) \qquad (6)$$

MeI reacted rapidly with 1^- to give quantitatively 2-methyl-2-phenylpropionitrile **6**. When MeI was added to an equimolar mixture of 1^- and **2** only 20% of 1^- was methylated and unchanged **1** was recovered, eqn. (5). These results confirmed that in the system $1^- + 2$ the equilibrium (1*b*) was shifted to the right and more than 80% of 1^- was reversibly attached to **2**, obviously in the form of the σ^H-adduct 12^-. When 1^- was added to a mixture of MeI and **2** *ca.* half of it was methylated. Thus the rate of methylation and the nucleophilic addition of 1^- to **2** appears similar. iv, What is the relationship between the rates of oxidation of the carbanion 1^- and the σ^H adduct **12**?

Since equilibrium (1*b*) is shifted to the right when 2 moles of 1^- + 1 mole of **2** were used, $[1^-]$ should be ≈ $[12^-]$.

$$1\text{ mole of }KMnO_4 + [2\text{ moles of }\mathbf{1}^- + 1\text{ mole of }\mathbf{2}] \xrightarrow[-70\,^\circ C,\ 2\text{ min.}]{NH_3\text{ liq.}} \mathbf{1}\ (0.16\text{ mol}) + \mathbf{3}\ (0.89\text{ mol}) + \mathbf{4}\ (0.17\text{ mol}) + \mathbf{5}\ (0.42\text{ mol}) \qquad (7)$$

When 1 mole of $KMnO_4$ was added to such a mixture **3** was the main product, eqn. (7). The result of eqn. (7) indicates that the oxidation of $\mathbf{12}^-$ occurs faster than $\mathbf{1}^-$.§ Taking into account that the crucial reactions discussed in this paper, the oxidation of $\mathbf{12}^-$ and $\mathbf{1}^-$ as well as the addition and alkylation of $\mathbf{1}^-$, are bimolecular it is possible to write the following relationship for the rate constants:

$$k_{\text{oxid. of }\mathbf{12}^-} > k_{\text{oxid. of }\mathbf{1}^-} > k_{\text{add. of }\mathbf{1}^- + \mathbf{2}} \approx k_{\text{MeI}+\mathbf{1}^-}$$

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Footnotes

† The notation A + [B + C] indicates that reagent A was added to a mixture of reagents B and C.

‡ In all the experiments the reaction mixtures were quenched with an excess of NH_4Cl. Yields are of the isolated products or determined by GC or GC/MS.

§ The molar ratio of **1**, **3**, **4** and **5** depends on the amount of $KMnO_4$. Nevertheless the major product was always **3**.

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