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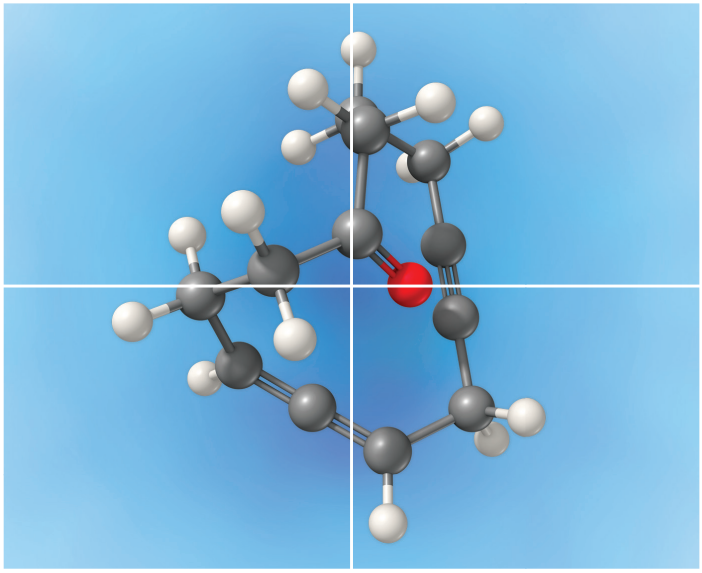

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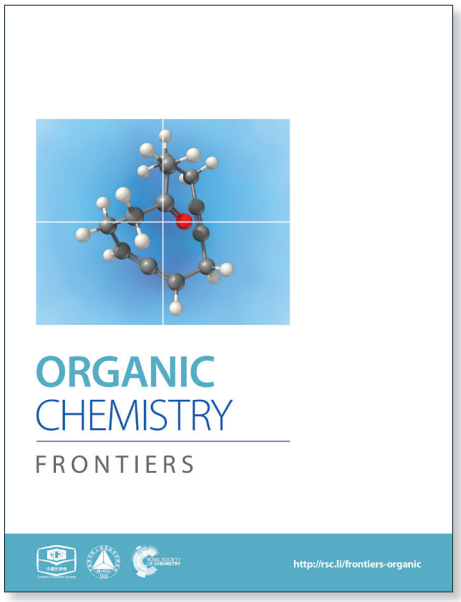

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ARTICLE

Reductive decyanation of malononitriles and cyanoacetates using photoactivated neutral organic super-electron-donors

Eswararao Doni[a] and John A. Murphy[a]*

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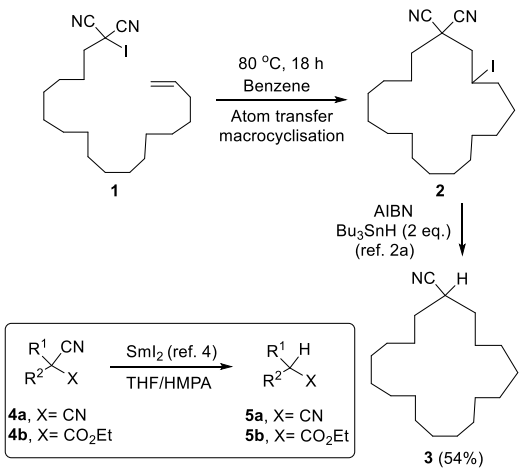
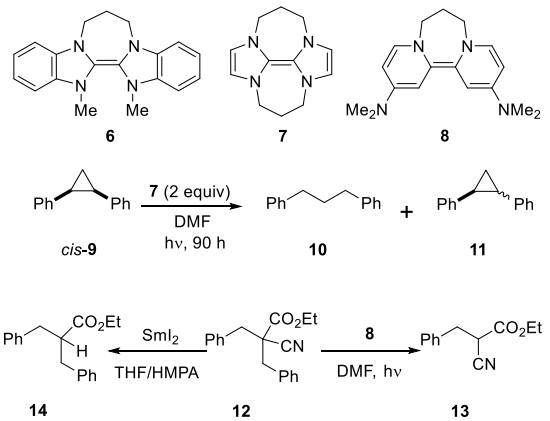
A metal-free reductive procedure for decyanation of malononitriles and cyanoacetates, using photoactivated organic electron donors, is described. Decyanation of cyanoacetates is more difficult than for malononitriles and it requires higher loading of the electron donor and extended reaction times. An anionic intermediate is proposed for the observed decyanations and a plausible mechanism is presented.

Introduction

Malononitriles have useful applications in both ionic[1] and radical[2] reactions. However, they are much less popular tools in organic synthesis than the closely related malonic esters, acetoacetates and sulfonyl acetates. This is partly because of the greater difficulty associated with the removal of the extra functional group in malononitriles *i.e.* a nitrile group, in comparison to a carboxyl or sulfonyl group in its relatives.[3] Accordingly, easier access to decyanation of malononitriles would encourage synthetic applications of malononitriles in organic chemistry. The reductive decyanation of malononitriles to mononitriles using tributyltin hydride/AIBN was discovered by Curran *et al.* [2a] during their studies on atom-transfer reactions of iodomalononitriles **1** and later, they made a full study of decyanation reactions.[3] Kang *et al.*[4] also reported the decyanation of both malononitriles **4a** and cyanoacetates **4b** using samarium (II) iodide/HMPA.



Scheme 1: Decyanation of malononitriles and cyanoacetates

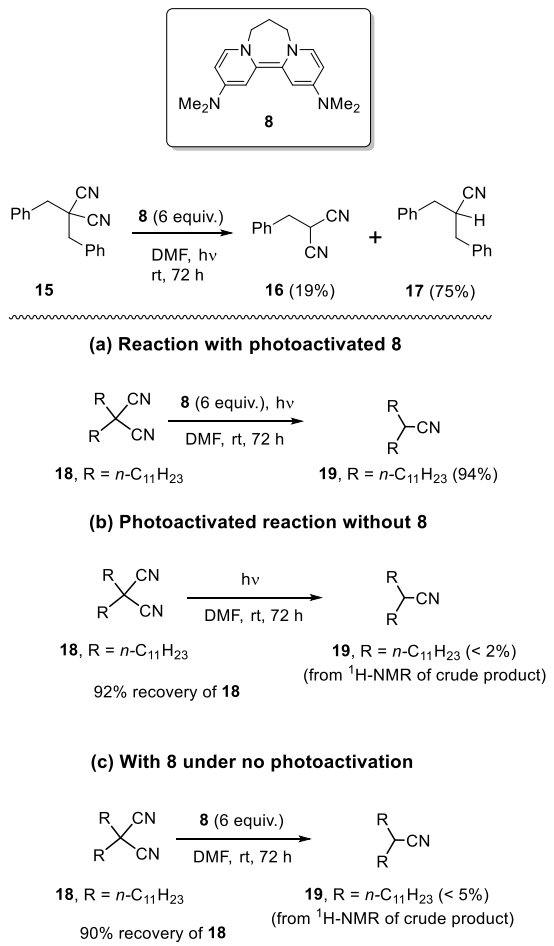


Scheme 2: Neutral organic electron donors and their reactivity.

We have recently developed a range of highly reactive neutral, organic super-electron-donors including **6**-**8** (Scheme 2).[5] These molecules donate one or two electrons to suitable substrates and thereby are oxidised to radical cations or dications respectively; the gain in aromaticity in the oxidised products contributes to the driving force for the electron donation. These electron donors perform difficult reduction reactions that are traditionally carried out by metals and metal complexes. For example, efficient single electron transfer (SET) from the donor **6** to unactivated aryl iodides generates the corresponding aryl radicals, while more powerful donors **7** and **8** generate the corresponding aryl anions via double electron transfer. Donors **7** and **8** also reduced arylsulfones,[5h] arenesulfonamides,[5h] Weinreb amides,[5g] acyloin derivatives,[5i] triflates and triflamides.[5l] More recently, we showed that photoactivation of the highly coloured donors **7** (vibrant yellow) and **8** (deep purple) enhanced their reducing power and that, under these conditions, they were able to reductively cleave Ar-Cl bonds in chloroarenes in high yields.[5k] These photoactivated donors were also able to reduce *cis*-1,2-

diphenylcyclopropane **9** to 1,3-diphenylpropane **10** along with epimerised starting material **11**.[5k]

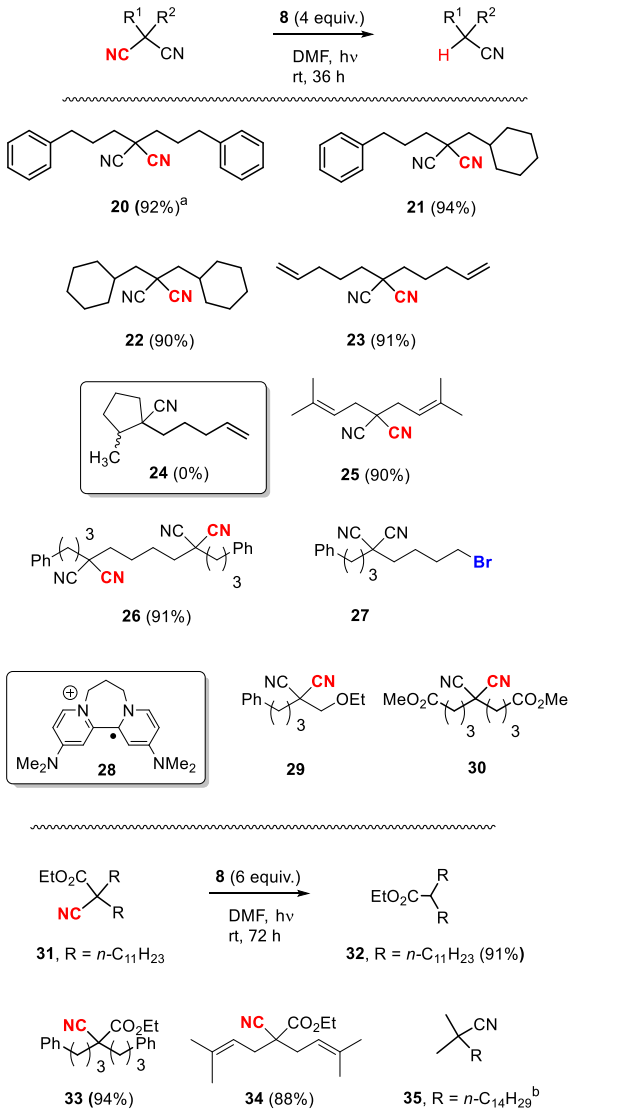
Very recently, we reported selective reduction of arenes over malonate esters and cyanoacetates.[5n] In that study, substrate **12** selectively provided benzylic C-C bond cleavage product **13**. This result was complementary to the earlier work by Kang *et al.*[4] in which the same substrate **12** provided decyanation product **14** upon treatment with SmI_2/HMPA. Our interest in decyanation reactions grew as there are very few reports of related chemistry in the literature and also the existing methods featured unfriendly reactions conditions such as using benzene as solvent, HMPA as additive or Bu_3SnH as reagent. A new decyanation reaction could be important in extending synthetic applications of malononitriles and, more generally, of nitriles in organic chemistry, and so we now report the results of our detailed study of these reactions.



Scheme 3: Reactions of photoactivated **8** with malononitriles **15** and **18**.

Results and Discussion

We firstly examined the malononitrile substrate **15** (Scheme 3). Surprisingly, the reaction provided both debenzylated product **16** (19%) and decyanation product **17** (75%) (Scheme 2). Decyanation of substrate **15** suggested that an electron donated from a photoactivated donor **8** targeted the nitrile groups instead of the arene ring in the substrate, but it was possible that the arene ring mediated the transfer. Thus, next, it was planned to test dialkyl malononitrile substrates with photoactivated **8**, rather than the usual benzyl substrates, to clarify the requirements of the decyanation process. In addition, we needed to establish that the decyanation resulted from photoexcitation of the donor **8**, and not from photoactivation of the substrate. We also needed reassurance that potential nucleophilic properties of the donor[5i] **8** played no role in the decyanation reaction. Compound **18** was selected as a test substrate and a set of three parallel reactions (Scheme 3) was carried out simultaneously, to address these points: (a) an original reaction of the substrate with photoactivated **8**, (b) a blank reaction under photoactivation conditions, but in the absence of **8** and (c) a blank reaction using **8**, but without photoactivation. To our delight, the original reaction (a) provided mononitrile product **19** in excellent yield (94%) while the blank reactions (b) and (c) provided very poor conversion (<2% and <5% respectively) of **18** to **19** but gave excellent recovery of starting material **18** (92% and 90% respectively) (Scheme 3).

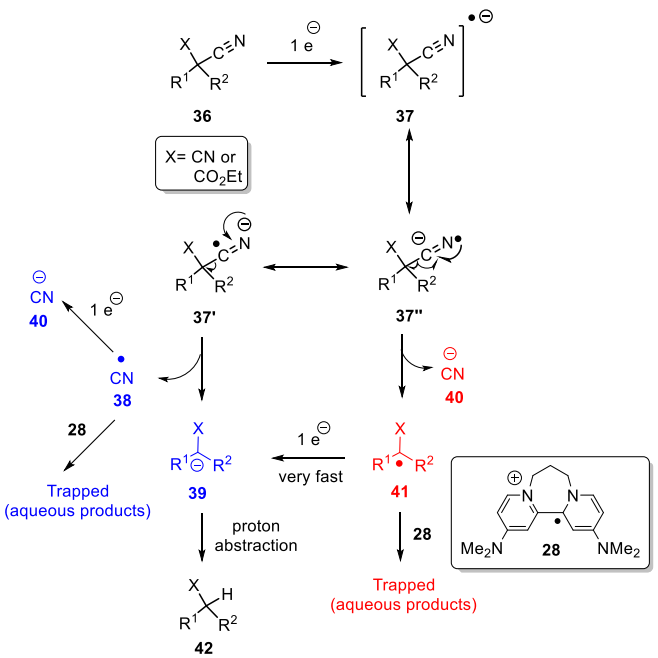


Scheme 4. Nitrile substrates for decyanation with super-electron-donor **8**. Cyano groups depicted in bold **red** underwent reductive decyanation. The values in parentheses are percent yields. [a] Reaction was carried out for 24 h. [b] This reaction gave recovered **35** (92%).

Therefore, the above reactions support electron-transfer as the mechanism for achieving decyanation reactions with photoactivated **8**. These results also show that the observed decyanation in **15** can occur without arene rings in the substrate. Encouraged by these results, we now optimised the reaction conditions. Reaction of **18** with photoactivated **8** (4 equiv.) (i) for 48 h provided complete consumption of **18** while (ii) 24 h reaction showed only 89% of conversion of **18** to **19**. Later, compound **18** was tested (iii) for 36 h, under the same reaction conditions and showed complete consumption of **18** and provided **19** in excellent isolated yields (92%), following column chromatography (see Table 1 in S.I.file).

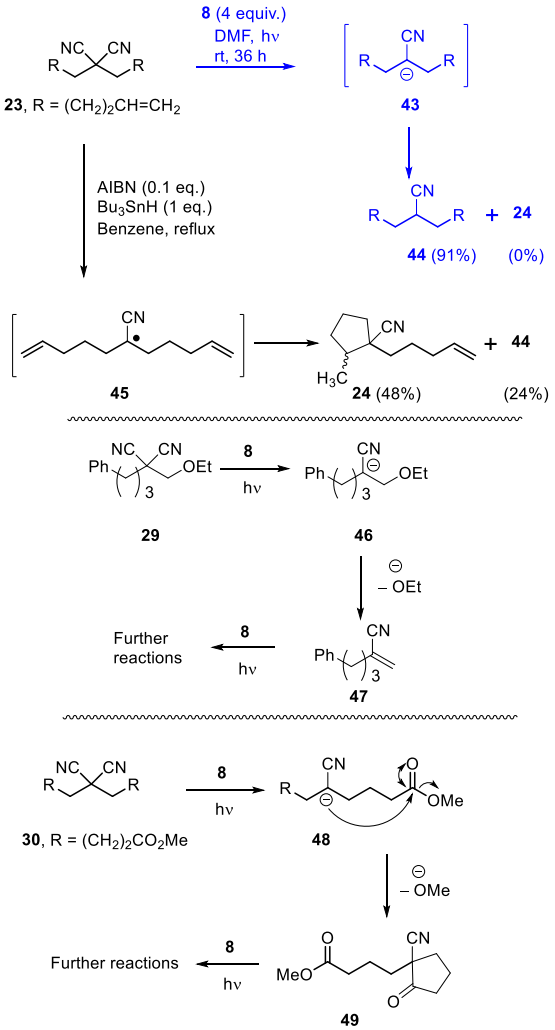
Once the optimisation was completed, a series of substrates was prepared and tested with photoactivated **8** and the results are shown in Scheme 4. Substrate **20** showed complete reaction within 24 h, and this faster reaction may be due to mediation of the electron transfer by the two phenyl rings. Substrates **21** and **22**, as expected, provided excellent yields of mononitrile products. Substrate **23** with suitably placed alkene groups for cyclisation provided exclusively uncyclised mononitrile product. However, the same compound **23**, under Bu_3SnH conditions[3] had provided both cyclised (**24**) and uncyclised products and this will be discussed later. Compound **25** afforded exclusive decyanation product and we did not observe any allylic C-C bond cleavage under our reaction conditions and alkene moieties were preserved in the decyanated product.

Compound **26** with two malononitrile groups provided decyanation at both sites. Compound **27**, featuring two electrophilic sites, (i) a malononitrile moiety and (ii) an alkyl bromide, provided a complete loss of starting material and no products were seen from ^{1}H-NMR analysis of the crude product. This likely results from selective reduction of the alkyl bromide to the corresponding radical intermediate, that is then trapped[5p] by the persistent radical-cation of the donor **28** to afford water-soluble products. Reactions of mechanistic probes **29** and **30** with photoactivated **8** showed complete consumption of starting materials but yielded complex mixtures of products. This will be discussed later.



Scheme 5. Proposed mechanism for the decyanation reactions.

After successful decyanation of malononitriles with photoactivated **8**, the process was now extended to the closely related cyanoacetates. Decyanation of cyanoacetates is a difficult task[6] compared to malononitriles and these reactions had not been successful with tributyltin hydride[3] but had worked well using SmI_2.[4] Firstly, dialkyl cyanoacetate **31** was tested with photoactivated donor **8** and it needed higher amounts of **8** (6 equiv.) along with extended reaction times (72 h) for the complete consumption of starting material but provided an excellent yield (91%) of decyanated product **32**. Substrates **33** and **34** were then tested under the same reaction conditions and they provided excellent yields of decyanated products as well. No allylic C-C bond cleavage was observed with **34** under our reaction conditions and the alkene moieties were preserved in the decyanated product (Scheme 4).



Scheme 6: Anionic intermediates are the key in the decyanation reactions.

Reductive decyanation of simple alkyl mononitriles is highly challenging due to the high C-CN bond dissociation energy (for comparison: 2,2-dimethylmalononitrile *vs*. isobutyronitrile = 78.9 *vs*. 126.5 kcal/mol).[6] The mononitrile substrates that underwent successful decyanation reactions by previous methods in the literature were mostly *tert*-alkyl nitriles, and the decyanation of these substrates was only achieved using solutions of solvated electrons formed from alkali metal.[7,8] Intrigued by this, we attempted

decyanation of *tert*-alkyl nitrile **35**. However, compound **35** completely resisted attack by our photoactivated **8** and provided recovery of **35** (92 %) (Scheme 4).

A plausible mechanism for the above decyanation reactions is shown in Scheme 5. Photoactivated **8** can donate an electron to substrate **36** (X = CN or CO_2Et) to form the radical-anion **37** and the radical-cation of the donor, **28**. The radical-anion **37** can fragment in two ways *i.e.* at **37'** to afford cyano radical **38** and stabilised alkyl anion **39** (pathway **A**, shown in blue) or at **37''** to afford cyanide anion **40** and alkyl radical **41** (pathway **B**, shown in red). This alkyl radical **41** can be trapped by the radical cation of the donor, **28**, to give water-soluble products, or it can quickly take a second electron from **8** and convert to stabilised alkyl anion **39**. The same applies for cyano radical **38** formed in the pathway **A** *i.e.* it can be trapped or further reduced to cyanide anion **40**. Finally, stabilised alkyl anion **39**, formed from either of pathways **A** and **B**, can pick up a proton. From our perspective, both routes are attractive, but what is clear is that under the strongly reductive environment in our reactions, electron-poor radicals are rapidly reduced.[5h]

Returning to discuss substrate **23**, it afforded exclusively the uncyclised decyanation product **44** under our reaction conditions. This result differs from Bu_3SnH case,[3] where the same **23** provided both the cyclised product **24** (major) and uncyclised product **44**, arising from radical intermediate **45**. So, in our study, we propose stabilised alkyl anion **43** as the key intermediate. As the yields of the reaction are high, trapping of radical intermediates by **28** has very little effect on these reactions and so, second electron transfer in pathway **B** should be very fast to convert alkyl radical **41** to alkyl anion **39**. Substrates **29** and **30** upon reaction with photoactivated **8** provided a complex mixture of products. Again, if an anionic intermediate is the key in these decyanations, these substrates should provide acrylonitrile derivative **47** and β-ketonitrile **49**, respectively, and both of these compounds can undergo further reactions or polymerisation under photoactivation conditions (Scheme 6).

Conclusions

In conclusion, decyanation of malononitriles and cyanoacetates is effected by neutral organic electron donor **8** under photoactivation. Decyanation of cyanoacetates is more difficult than malononitriles under our reaction conditions, but also proceeds in excellent yields. We propose that stabilised anionic intermediates are the key for these reactions. These reactions have parallels with chemistry induced by SmI_2, where decyanation of malononitriles also affords anionic intermediates (no 5-*exo* cyclisation of intermediates onto alkenes was seen).[4] Both types of reaction are conducted at room temperature in the presence of excess reducing agent. However, in the case of SmI_2, the presence of HMPA is needed.[4] Thus, the current organic electron donors represent an easily prepared and convenient reagent for decyanation of malononitriles and cyanoacetates.

Acknowledgements

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Dedication.

This paper is dedicated to Professor Max Malacria on the occasion of his 65th birthday.

Notes and references

[a] WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow G1 1XL (UK). E-mail: john.murphy@strath.ac.uk.

Electronic Supplementary Information (ESI) available: [experimental procedures and analyses, together with the NMR spectra of key compounds]. See DOI: 10.1039/b000000x/

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