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Reduction of nitroarenes, azoarenes and hydrazine derivatives by an organic super electron donor

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ABSTRACT

Reduction of nitrobenzene by excess organic electron donor, **12**, affords diphenylhydrazine in a reaction where azobenzene oxide and azobenzene are likely intermediates. No cleavage of the N-N σ-bond is seen under photoactivation conditions, whereas traces are seen under thermal activation. Hydrazone derivatives were prepared to explore the cleavage of N-N σ-bonds; the results show that a low-lying LUMO assists the transition state for accepting an electron, and the stabilisation that the potential fragments from N-N bond cleavage afford to the fragments is important in determining whether cleavage is observed.

1. Introduction

Nitrobenzenes **1** are versatile substrates for synthesis, undergoing easy reduction to anilines **4** via monoaryl compounds **2**–**4** (Scheme 1), and/or compounds arising from the coupling of intermediates, **5**–**8** [1,2]. The reaction conditions and reagents are important in determining the products, as they provide reactive species at different rates and therefore different concentrations, which is important for coupling. In terms of closed-shell intermediates, nitroso compounds **2** can dimerise to form diazene dioxides **5** or can condense with hydroxylamines **3** to afford azoxides **6**, or with anilines **4** to afford azo-compounds **7**, while electron transfer–based reductions could also access these coupled compounds via radical intermediates. Further reduction to diarylhydrazines **8** can then follow [1].

Despite the extensive interest in reduction of nitro groups, no reduction of nitro groups in the absence of redox-active metals with organic electron donors has yet been recorded [9], although Hu et al. [1] explored the reduction of nitrobenzenes to anilines **4** by electron transfer, using samarium and the organic mediator 1,1′-dioctyl-4,4′-bipyridinium dibromide.

Organic electron donors have been widely studied in recent years, and their ability to behave as strong reducing agents has been established [3,4]. An easily accessible donor is DMAP-derived donor **12**; this is prepared by treatment of the precursor salt **9** with two equivalents of base (Scheme 2). When it acts as a donor, sequential transfer of two electrons from **12** affords the aromatic disalt, **14**. Compound **12** is deep purple in colour with an absorption maximum around 365 nm, making it convenient for photoactivated reactions without specialist photochemical equipment. This affords the opportunity for promotion of an electron from HOMO to LUMO. Photoexcited **12** is therefore even more reducing than the ground state counterpart [3i]. The experiments reported in this paper started by probing the reactivity of electron donor **12** with nitrobenzene under both photoactivated and thermal conditions.

2. Results

Nitrobenzene was treated with disalt **9**, (X = I) and NaH as base under photoactivated conditions (365 nm) at ambient temperature as shown in Table 1 (entries 1–4). Full reduction from nitrobenzene to aniline requires 6 electrons (+corresponding protons – see below); these could be provided by 3 equivalents of donor **12**, which would require treatment of salt **9** (3 eq) with NaH (6 eq) as in entry 1. This experiment led to isolation of 1,2-diphenylhydrazine **18** cleanly, but to no aniline **19**. Clearly, conditions were favourable for intermediates to couple. Progressively decreasing the

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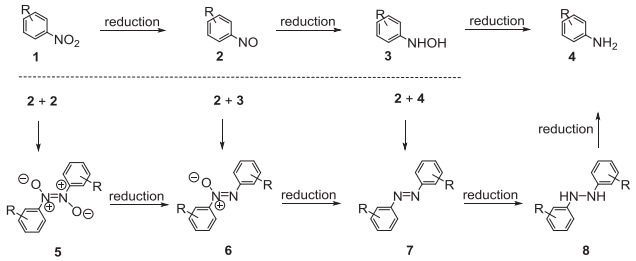
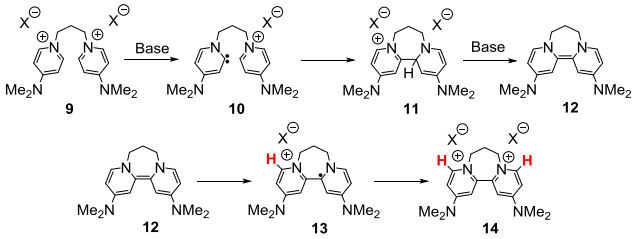


Scheme 1. Reduction of nitroarenes.



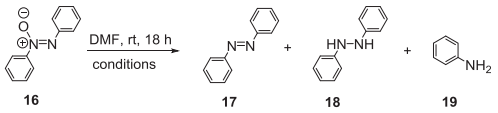
Scheme 2. Preparation and reaction of electron donor **12**.

amount of reducing agent reacted with substrate **15** allowed us to probe for potential intermediates *en route* to **18** and led to the results in Table 1 (entries 2–4). The results show that in the presence of limited equivalents of **9** (1 eq, entry 4), azoxide **16** (60%) is formed as the exclusive product. Increasing the number of equivalents of **9** to 1.5 gave rise to azobenzene **17** (68%), while a further increase in reducing equivalents yielded diphenylhydrazine **18**. The presence of the DMAP-derived salt **9** was essential, as the same reaction run without the salt led to no reaction. These outcomes from the photoactivation conditions were compared with thermal activation (Table 1, entry 5) also using NaH (6 eq) and salt **9** (3 eq), which provided diphenylhydrazine **18** (45%) as the major product, together with azobenzene **17** (14%) and a small amount of aniline **19** (4%).

These results are consistent with the formation of **18** through a sequential series of reductions, with **16** and **17** as intermediates.

To check whether this scheme was reasonable, the various individual products were tested for their reactivity. Firstly, azoxybenzene **16** was reacted with donor **12** formed *in situ*, according to the conditions shown in the experiments in Table 2 using precursor salt **9** in the presence of NaH. In the presence of excess of the reducing agent and under photochemical activation (Table 2, entries 1 and 2), azoxybenzene was reduced principally to hydrazobenzene **18**, while azobenzene **17** was the minor product. When

Table 2
Reduction of azoxybenzene **16** by donor **12**, formed *in situ*.



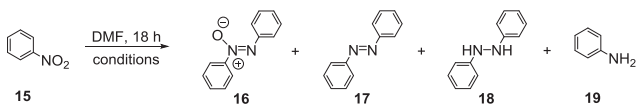
Entry	Reduction of **16** as in scheme conditions	**16**	**17**	**18**	**19**
1	NaH (6 eq), UV irradiation, rt, **9** (X = I), (3 eq)	0	18	73	0
2	NaH (4 eq), UV irradiation, rt, **9** (X = I), (2 eq)	0	20	70	0
3	NaH (2 eq), UV irradiation, rt, **9** (X = I), (1 eq)	0	80	5	0
4	NaH (6 eq), 130 °C, **9** (X = I), (3 eq)	0	82	traces	0

just 1 equivalent of the reducing agent **12** was present (entry 3), then azobenzene was the dominant product (80%), while a trace (5%) of hydrazobenzene was isolated. When the reaction was repeated with excess of reducing agent (entry 4), but under thermal rather than photochemical activation, azobenzene was the major product (82%).

To check that azobenzene **17** can be reduced to diphenylhydrazine **18** under the photoactivated conditions, it was subjected to the reaction in the presence of varying amounts of [disalt **9** + NaH], leading to uniformly high yields of **18** (Table 3, entries 1–3). In these reactions, formation of aniline **19** was not observed, even when there was an excess of electrons available. When the reduction of azobenzene **17** was conducted under thermal conditions, diphenylhydrazine **18** was again the major product, but aniline was produced in low yield (4%) consistent with thermal fragmentation of an N-N bond, perhaps in the dianion of **18**. Although photoactivation leads to a more powerful reducing system than the thermal activation, this dianion of **18** should be very difficult to reduce, so that, in the absence of thermal fragmentation, further progress towards aniline **19** would rely on conversion of this dianion to a less negatively charged species (see below).

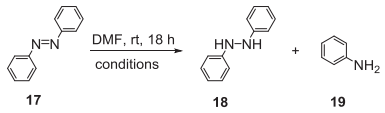
For formation of products **17**, **18** from nitrobenzene, a coupling of two intermediates is needed, involving the formation of an N-N bond. Scheme 1 shows three stages at which dimerization could occur, and all involve nitrosobenzene. At this stage, we do not know if all three ways of forming the N-N bond contribute to the product, or indeed if open-shell intermediates are active in the coupling. Besides the N-N bond formation, oxygen atoms must be removed to arrive at **17** and **18**. Scheme 3 shows two ways in which products arising from the electron donor **12** can assist. The first deals with protonation. Under our conditions, just sufficient NaH is used to deprotonate **9** and form **12**; when donor **12** transfers two electrons, dication **14** is formed, featuring somewhat acidic protons, *ortho* to the pyridinium nitrogen [3f]. Dianion

Table 1
Reduction of nitrobenzene by donor **12**, formed *in situ*.



Entry	Reduction of **15** as in scheme conditions	**16** (%)	**17** (%)	**18** (%)	**19** (%)
1	NaH (6 eq), UV irradiation, rt, **9** (X = I), (3 eq)	0	0	84	0
2	NaH (4 eq), UV irradiation, rt, **9** (X = I), (2 eq)	0	23	59	0
3	NaH (3 eq), UV irradiation, rt, **9** (X = I), (1.5 eq)	0	68	0	0
4	NaH (2 eq), UV irradiation, rt, **9** (X = I), (1 eq)	60	<1	0	0
5	NaH (6 eq), 130 °C, **9** (X = I), (3 eq)	0	14	45	4

Table 3
Reduction of azobenzene **17**.



Entry	Reduction of **17** as in scheme conditions	Recovered **17**	**18**	**19**
1	NaH (6 eq), UV irradiation, rt, **9** (X = I), (3 eq)	0	89	0
2	NaH (4 eq), UV irradiation, rt, **9** (X = I), (2 eq)	0	90	0
3	NaH (2 eq), UV irradiation, rt, **9** (X = I), (1 eq)	8	79	0
4	NaH (6 eq), 130 °C, **9** (X = I), (3 eq)	12	72	4

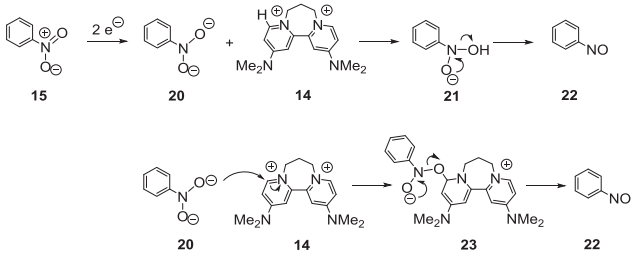
20, a likely intermediate in the reduction of nitrobenzene, could be protonated to **21**, which would then collapse to nitrosobenzene. A similar proton transfer could occur, employing radical cation **13** (the structure is shown in Scheme 2) rather than dication **14**.

Alternatively, rather than being deprotonated, intermediates **13** and/or **14** could be attacked by nucleophiles in the position *ortho* to the pyridine nitrogen. In this case, dianion **20** would afford **23**, fragmentation of which could yield nitrosobenzene **22**. Scheme 3 shows dianion **20** as the reactive intermediate, but analogous solutions could be proposed for any negatively charged intermediate that needs to shed a leaving group.

In our experiments above, no N-N σ-bond cleavage was observed by electron donor **12** at ambient temperature under photoactivated conditions. An area of great current interest involves reducing molecular nitrogen to ammonia with electron donors [5]; the first steps would involve reduction of the π-bonds, but a really challenging part of the process would involve cleavage of the N-N σ-bond of hydrazine or a derivative. Accordingly, we determined to understand whether N-N σ-bonds were intrinsically too difficult to cleave, and to what extent their cleavage is facilitated by substituents. In the experiments above, cleavage might have been impeded due to charge (*e.g.* in reduction of **17**, we would expect the dianion of **18** to form, but further reduction of that charged derivative leading to N-N bond cleavage would likely be impossible due to the charge; this charge could potentially be mitigated through either of the processes in Scheme 3, employing the dianion **18** as reactive intermediate instead of **20**).

The fact that N-N σ-bond cleavage was not seen following activation by our photoactivated donor **12** now led us to explore the factors that might influence cleavage of such bonds. Accordingly, we prepared a series of hydrazine derivatives **24**–**27** [5].

Reduction of these compounds should be assisted if a low energy π* or σ* orbital is available to house an electron from the electron donor. Following acceptance of an electron, cleavage of the N-N bond in the radical anion would be facilitated by substituents



Scheme 3. Possible routes for oxygen atom removal.

on the N atoms that would stabilise the resulting fragments, the radical and the anion. Hence the easiest of our substrates to cleave should be the tetraphenylhydrazine **24**.

Indeed, it is seen that **24** was reductively cleaved to afford diphenylamine **28** in excellent yield under either photochemical or thermal activation (Table 4, entries 1 and 2 respectively). Substrate **25** still should have a low-lying LUMO associated with the diphenylamino group; however, the cleavage of a radical anion of this substrate should be more challenging than in the radical anion of **24**, as the resulting piperidonyl anion or radical will be less stabilised that the corresponding diphenylaminyl species from **24**. This was borne out by experiment - substantial amounts of starting material were recovered under both photoactivation and thermal activation, but a greater amount of recovered starting material was seen in the thermal activation case (87% *vs.* 56%); correspondingly, whereas **28** was isolated, albeit in low yield (35%) from the photoactivation, the thermal activation afforded no such product. Compound **26** underwent cleavage to afford a low yield of diphenylamine (18%) under our standard photoactivation conditions (18 h). It is noteworthy that extending the time of the photoactivation for **25** and **26** to 36 h, did not lead to increased yields over the shorter duration experiments.

Similarly, increasing the number of equivalents of electron donor to six, had no effect on the outcome of the photoactivation reactions of **25** and **26**. [Piperidone or piperidine respectively, were not isolated from these reactions. Performing repeat experiments in which defined amounts of piperidine and piperidone were added just prior to workup also did not lead to their isolation; we attribute this to volatility and water solubility].

3. Conclusions

Reduction of nitrobenzene by sufficient numbers of equivalents of organic electron donor, **12**, affords diphenylhydrazine; less equivalents of reducing agent afford azobenzene oxide or azobenzene. No cleavage of the N-N σ-bond is seen under photoactivation conditions, whereas traces are seen under thermal activation. Efforts to cleave N-N σ-bonds in hydrazine derivatives show that a low-lying LUMO can assist the transition state for accepting an electron, and the structure of the potential fragments from N-N bond cleavage affects that cleavage.

4. Experimental section

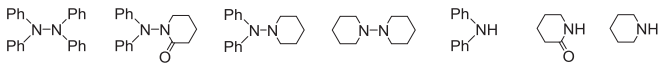
4.1. General information

All reagents were commercially available and used without additional purification.^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent on a Bruker AV3 at 400 and 100 MHz, respectively, and the NMR chemical shifts are reported in ppm downfield from an internal solvent peak. Signal multiplicities are abbreviated as: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintuplet; m, multiplet; bs, broad singlet; tt, triplet of triplets. Coupling constants are given in Hertz (Hz).

Thin layer chromatography (TLC) was performed using aluminium-backed sheets of silica gel and visualized under a UV lamp (254 nm). TLCs were revealed with phosphomolybdic acid. Column chromatography was performed to purify compounds by using silica gel 60 (200–400 mesh).

The electron transfer reactions were carried out within a glove box (Innovative Technology Inc., USA) under nitrogen atmosphere. All solvents or samples introduced into the glovebox were transferred through the port, which was evacuated and purged with nitrogen ten times before entry. When the reaction mixtures were

Table 4
Reduction of hydrazines and derivatives.



24 25 26 27 28 29 30

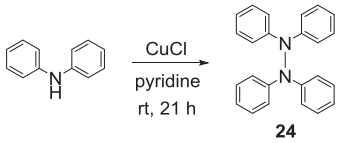
Entry	Conditions (in salt **9**, X = I)	Substrate	Recovered substrate	**28**	**29**	**30**
1	NaH (6 eq), UV irradiation, rt, **9**, (3 eq)	24	0	89	–	–
2	NaH (6 eq), 130 °C, **9**, (3 eq)	24	0	90	–	–
3	NaH (6 eq), UV irradiation, rt, **9**, (3 eq) 18 h	25	56	35	–	–
4	NaH (6 eq), 130 °C, **9**, (3 eq)	25	87	traces	–	NA
5	NaH (6 eq), UV irradiation, rt, **9**, (3 eq) 18 h	26	66	18	NA	–
6	NaH (6 eq), 130 °C, **9**, (3 eq)	26	94	0	NA	–
7	NaH (6 eq), UV irradiation, rt, **9**, (3 eq) 36 h	25	55	40	–	NA
8	NaH (6 eq), UV irradiation, rt, **9**, (3 eq) 36 h	26	53	23	NA	–
9	NaH (12 eq), UV irradiation, rt, **9**, (6 eq) 18 h	25	58	36	–	NA
10	NaH (12 eq), UV irradiation, rt, **9**, (6 eq) 18 h	26	65	21	NA	–
11	NaH (6 eq), UV irradiation, rt, **9**, (3 eq) 18 h	27	70	NA	NA	0
12	NaH (6 eq), 130 °C, **9**, (3 eq)	27	70	NA	NA	0

prepared, the reaction vessel was removed from the glovebox and the rest of the reaction was performed in a fumehood under UV radiation or thermal conditions. All the UV reactions were carried out by using two focused UV lamps with filters (λ = 365 nm, each 100 W) placed opposite to each other, around the Pyrex reaction flask, at room temperature.

Infra-Red spectra were recorded on an ATR-IR spectrometer. Melting points were determined on a Gallenkamp Melting point apparatus. High-resolution mass spectrometry (HRMS) was performed at Swansea University, in the EPSRC National Mass Spectrometry Centre. Accurate mass was obtained using atmospheric pressure chemical ionisation (APCI), chemical ionisation (CI), electron ionisation (EI), electrospray ionisation (ESI) or nanospray ionisation (NSI) with a LTQ Orbitrap XL mass spectrometer.

4.2. Synthesis of hydrazine derivatives

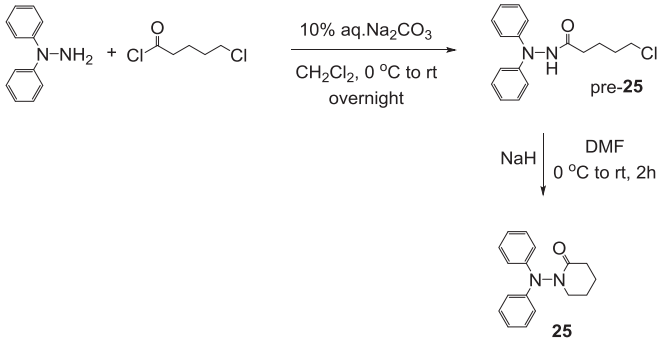
4.2.1. Tetraphenylhydrazine (*24*)[6a]



24

To a 250 mL 3-necked round-bottomed flask, under argon, were added copper chloride (1.98 g, 20.0 mmol) and pyridine (50 mL). The atmosphere of the flask was replaced by oxygen and a solution of diphenylamine (1.69 g, 9.99 mmol) in pyridine (10 mL) was added to the flask upon vigorous stirring and oxygen flow. After addition, the mixture was stirred at room temperature for 21 h under oxygen atmosphere. Pyridine was removed by distillation and the resulting residue was extracted with Et_2O (4 × 25 mL), the combined organic extracts were dried over Na_2SO_4, filtered and concentrated to afford the crude product. Purification was made by column chromatography on silica using DCM (25%) in hexane to afford tetraphenylhydrazine **24** as a white powder (184.9 mg, 0.55 mmol, 11%). M. Pt. 144–146 °C (lit. 144–147 °C) [7] δ_H (400 MHz, $CDCl_3$): 6.90 (4H, tt, J = 7.2, 1.2 Hz, Ar*H*), 7.22–7.17 (8H, m, Ar*H*), 7.32–7.29 (8H, m, Ar*H*).δ_C (100 MHz, $CDCl_3$): 118.3, 122.2, 129.2, 143.7. IR (NEAT) ν (cm^{-1}) = 689, 740, 1030, 1273, 1294, 1485, 1586. *m/z* (APCI) calcd. for $C_{24}H_{21}N_2$ $[M+H]^+$: 337.1699, found: 337.1696.

4.2.2. 1-(Diphenylamino)piperidin-2-one (*25*)

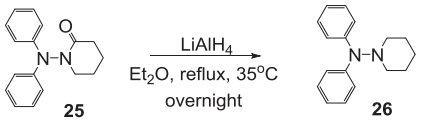


To a 50 mL round-bottomed flask at 0 °C, *N,N*-diphenylhydrazine **24** (500 mg, 2.72 mmol), CH_2Cl_2 (10 mL) and a solution of Na_2CO_3 (10% in water, 10 mL) was added. After stirring for 5 min, 5-chlorovaleroylchloride (545 mg, 3.54 mmol) was added dropwise to the mixture. The reaction mixture was stirred and allowed to warm from 0 °C to room temperature overnight. The mixture was extracted with CH_2Cl_2 (4 × 15 mL), the combined organic extracts were washed once with water, dried over Na_2SO_4, filtered and concentrated to afford the crude product. Purification was made by column chromatography on silica using EtOAc (10%) in hexane to afford 5-chloro-*N*′,*N*′-diphenyl-pentanehydrazide (pre-**25**) as a brown powder (558 mg, 1.85 mmol, 68%, as two rotamers). M. Pt. 115–117 °C δ_H (400 MHz, $CDCl_3$): 1.74 (maj.) (4H, m, 2 × C*H*$_2$), 1.86 (min.) (4H, m, 2 × C*H*$_2$), 2.31 (min.) (2H, t, J = 7.2 Hz, C*H*$_2$), 2.46 (maj.) (2H, t, J = 7.2 Hz, C*H*$_2$), 3.46 (maj.) (2H, t, J = 6.0 Hz, C*H*$_2$), 3.56 (mi.) (2H, t, J = 6.0 Hz, C*H*$_2$), 7.04 (min.) (2H, m, Ar*H*), 7.10–7.14 (min. + maj.) (4H, m, Ar*H*), 7.27–7.37 (min. + maj.) (4H, m, Ar*H*), 7.49 (maj.) (1H, s, Ar*H*), 7.89 (min.) (1H,s, Ar*H*). δ_C (100 MHz, $CDCl_3$): 20.9 (ma.), 22.2 (mi.), 29.9 (ma.), 31.4 (mi.), 31.5 (ma.), 32.7 (mi.), 44.0 (mi. + ma.), 118.8 (ma.), 118.9 (mi.), 122.6 (mi.), 123.3 (ma.), 128.7 (mi.), 129.0 (ma.), 145.4 (mi.), 145.5 (ma.), 170.9 (mi.), 177.1 (ma.). IR (NEAT) ν (cm^{-1}) = 640, 705, 750, 1324, 1450, 1487, 1587, 1263, 2363, 3266. HRMS (CI): calcd. for $C_{17}H_{20}ON_2Cl$ ($[M+H]^+$): 303.1259, found: 303.1261.

NaH (60 mg, 2.5 mmol) was added to a 100 mL round-bottomed flask inside a glovebox under nitrogen atmosphere. Then, a solution of 5-chloro-*N*′,*N*′-diphenylpentanehydrazide, pre-**25** (550 mg, 1.82 mmol) in 20 mL of anhydrous DMF, was added dropwise to the

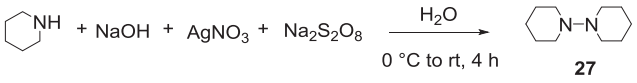
flask at 0 °C and the mixture was stirred and allowed to warm from 0 °C to room temperature for 2 h. Then, NaH was quenched by isopropanol (3 mL) and water. The mixture was extracted with EtOAc (4 × 20 mL), the combined organic extracts were washed once with water, dried over Na_2SO_4, filtered and concentrated to afford *N,N*-diphenyl-piperidone **25** as a brown powder (470 mg, 1.76 mmol, 97%). M. Pt. 90–92 °C δ_H (400 MHz, $CDCl_3$): 1.90 (2H, m, CH_2), 2.01 (2H, m, CH_2), 2.60 (2H, t, $J = 6.4$ Hz, CH_2), 3.67 (2H, t, $J = 6.4$ Hz, CH_2), 7.03 (2H, tt, $J = 7.2$, 1.2 Hz, Ar*H*), 7.11–7.13 (4H, m, Ar*H*), 7.28–7.32 (4H, m, Ar*H*). δ_C (100 MHz, $CDCl_3$): 20.6, 23.4, 32.8, 48.9, 118.7, 122.2, 128.8, 143.2, 168.7. IR (NEAT) ν (cm^{-1}) = 642, 690, 741, 947, 1302, 1325, 1406, 1491, 1585, 1655, 2357, 2936. HRMS (CI): calcd for $C_{17}H_{19}ON_2$ ($[M+H]^+$): 267.1492, found: 267.1493.

4.2.3. 1-(diphenylamino)piperidine (**26**)



$LiAlH_4$ (45 mg, 1.19 mmol), *N,N*-diphenyl-piperidone **25** (240 mg, 0.90 mmol) and dry diethyl ether (20 mL) were added to a 100 mL 3-necked round-bottomed flask under argon. The reaction mixture was refluxed at 35 °C overnight. Then $LiAlH_4$ was cautiously quenched by addition of isopropanol and then water. The precipitate was filtered off and the filtrate was washed twice with water, dried over Na_2SO_4, filtered and concentrated to afford the crude product. Purification was made by column chromatography on silica eluting with EtOAc (2%) in hexane to afford 1-*N,N*-diphenylaminopiperidine **26** a white solid (170 mg, 0.67 mmol, 75%). M. Pt. 55–57 °C δ_H (400 MHz, $CDCl_3$): 1.33 (2H, quint. $J = 6.0$ Hz, CH_2), 1.75 (4H, quint., $J = 5.6$ Hz, 2 × CH_2), 2.69 (4H, t, $J = 5.2$ Hz, 2 × CH_2), 7.04-7-09 (6H, m, Ar*H*), 7.28–7.34 (4H, m, Ar*H*). δ_C (100 MHz, $CDCl_3$): 23.2, 26.1, 52.6, 121.7, 122.0, 128.4, 143.9. IR (NEAT) ν (cm^{-1}) = 690, 748, 866, 1314, 1443, 1487, 1585, 2938. HRMS (CI): calcd. for $C_{17}H_{21}N_2$ ($[M+H]^+$): 253.1699, found: 253.1702.

4.2.4. Bipiperidine (**27**) [5b]



Piperidine (2.5 g, 29.4 mmol), NaOH (2.35 g, 58.8 mmol), H_2O (15 mL) and $AgNO_3$ (250.0 mg, 1.47 mmol). were added to a 100 mL round-bottomed flask at 0 °C. After stirring for 15 min, a solution of $Na_2S_2O_8$ (6.99 g, 29.4 mmol) in H_2O (20 mL) was added to the mixture which was then stirred from 0 °C to room temperature for 4 h. The mixture was extracted with EtOAc (3 × 30 mL), the combined organic extracts were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography on silica eluting with EtOAc (10%) in hexane to afford bipiperidine **27** as a yellow oil (1.29 g, 7.64 mmol, 52%). δ_H (400 MHz, $CDCl_3$): 1.34 (4H, m, CH_2), 1.59 (8H, m, CH_2), 2.66 (8H, t, $J = 5.2$ Hz, CH_2). δ_C (100 MHz, $CDCl_3$): 24.9, 26.7, 49.3. IR (NEAT) ν (cm^{-1}) = 875, 1442, 2731, 2800, 2852, 2930. *m/z* (EI) $C_{10}H_{20}N_2$ [M]: 168.1.

4.3. General reduction procedures

Inside a glovebox under nitrogen atmosphere, a pressure tube was loaded with DMAP salt **9** (specified amount), dry DMF (5 mL), NaH (specified amount) and reduction substrate (0.33 mmol). The tube was sealed, taken outside the glovebox and the mixture was stirred for 18 h at room temperature under UV light OR at 130 °C without UV light, as indicated. The mixture was quenched at room temperature with water (30 mL), extracted with Et_2O (2 × 25 mL), the combined organic extracts were washed with water (3 × 25 mL), dried over Na_2SO_4, filtered and concentrated. Crude products were purified by column chromatography on silica eluting with EtOAc (5%) in hexane, for isolation of azobenzene **17**, azoxybenzene **16** and diphenylamine **28**, and with EtOAc (20%) in hexane for isolation of hydrazine **18**.

4.3.1. Reduction of nitrobenzene **15**

4.3.1.1. Table 1, entry 1. Nitrobenzene **15** (41 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford, following work-up and chromatography, 1,2-diphenylhydrazine **18** as a white solid (25.8 mg, 0.14 mmol, 84%). M.Pt. 123–125 °C (lit. 124–125 °C) [7] $\boldsymbol{\delta}_H$ (400 MHz, $CDCl_3$): 5.62 (2H, bs, N*H*), 6.87–6.82 (6H, m, Ar*H*), 7.24–7.19 (4H, m, Ar*H*). $\boldsymbol{\delta}_C$ (100 MHz, $CDCl_3$): 112.5, 120.1, 129.5, 149.0. IR (NEAT) ν (cm^{-1}) = 689, 775, 927, 1072, 1454, 1483. *m/z* (NSI) calcd for $C_{12}H_{13}N_2$ $[M+H]^+$: 185.1073, found: 185.1073.

4.3.1.2. Table 1, entry 2. Nitrobenzene **15** (41 mg, 0.33 mmol) was treated with DMAP salt **9** (356.6 mg, 0.66 mmol) and sodium hydride (31.7 mg, 1.32 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford 1,2-diphenylhydrazine **18** (17.9 mg, 0.10 mmol, 59%), NMR spectra details as above, and azobenzene **17** as an orange solid (6.9 mg, 0.04 mmol, 23%). M. Pt. 65–66 °C (lit. 65–66 °C) [2g]. $\boldsymbol{\delta}_H$ (400 MHz, $CDCl_3$): 7.55–7.46 (6H, m, Ar*H*), 7.94–7.90 (4H, m, Ar*H*). $\boldsymbol{\delta}_C$ (100 MHz, $CDCl_3$): 123.0, 129.2, 131.1, 152.8. IR (NEAT) ν (cm^{-1}) = 688, 775, 927, 1072, 1454, 1483. *m/z* (EI) $C_{12}H_{10}N_2$ [M]: 182.1.

4.3.1.3. Table 1, entry 3. Nitrobenzene **15** (41 mg, 0.33 mmol) was treated with DMAP salt **9** (267.4 mg, 0.50 mmol) and sodium hydride (23.8 mg, 0.99 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford azobenzene **17** (20.4 mg, 0.11 mmol, 68%). NMR spectra details as above.

4.3.1.4. Table 1, entry 4. Nitrobenzene **15** (41 mg, 0.33 mmol) was treated with DMAP salt **9** (178.3 mg, 0.33 mmol) and sodium hydride (15.8 mg, 0.66 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford azoxybenzene **16** as a yellow oil (19.6 mg, 0.10 mmol, 60%). $\boldsymbol{\delta}_H$ (400 MHz, $CDCl_3$): 7.39 (1H, tt, $J = 6.8$, 1.2 Hz, Ar*H*), 7.59–7.47 (5H, m, Ar*H*), 8.18–8.15 (2H, m, Ar*H*), 8.33–8.30 (2H, m, Ar*H*). $\boldsymbol{\delta}_C$ (100 MHz, $CDCl_3$): 122.5, 125.7, 128.9, 129.0, 129.8, 131.7, 144.2, 148.5. IR (NEAT) ν (cm^{-1}) = 686, 764, 1277, 1301, 1441, 1476. *m/z* (NSI) calcd for $C_{12}H_{11}N_2O$ $[M+H]^+$: 199.0866, found: 199.0865. A trace amount of azobenzene **17** was also observed in the ^1H NMR spectra of the crude product.

4.3.1.5. Table 1, entry 5. Nitrobenzene **15** (40.6 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at 130 °C for 18 h to afford azobenzene **17** (3.3 mg, 0.02 mmol, 11%), 1,2-diphenylhydrazine **18** (13.7 mg, 0.07 mmol, 45%), NMR spectra details as above, and aniline **19** (1.2 mg, 0.01 mmol, 4%), yields were quantified by use of 1,3,5-trimethoxybenzene as an internal NMR standard. Observed ^1H NMR for aniline **19**: $\boldsymbol{\delta}_H$ (400 MHz, $CDCl_3$): 3.05 (2H, s, NH_2), 6.70–6.67 (2H, m, Ar*H*), 6.76 (1H, t, $J = 7.6$ Hz, Ar*H*), 7.17–7.13 (2H, m, Ar*H*); data were in accordance with literature.

4.3.2. Reduction of azoxybenzene ***16***

4.3.2.1. Table 2, entry 1. Azoxybenzene **16** (65.4 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford azobenzene **17** (11 mg, 0.06 mmol, 18%) and 1,2-diphenylhydrazine **18** (44 mg, 0.24 mmol, 73%). NMR spectra details as above.

4.3.2.2. Table 2, entry 2. Azoxybenzene **16** (65.4 mg, 0.33 mmol) was treated with DMAP salt **9** (356.6 mg, 0.66 mmol) and sodium hydride (31.7 mg, 1.32 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford azobenzene **17** (12 mg, 0.066 mmol, 20%) and 1,2-diphenylhydrazine **18** (42.5 mg, 0.23 mmol, 70%). NMR spectra details as above.

4.3.2.3. Table 2, entry 3. Azoxybenzene **16** (65.4 mg, 0.33 mmol) was treated with DMAP salt **9** (178.3 mg, 0.33 mmol) and sodium hydride (15.8 mg, 0.66 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford azobenzene **17** (48 mg, 0.26 mmol, 80%) and 1,2-diphenylhydrazine **18** (3 mg, 0.017 mmol, 5%). NMR spectra details as above.

4.3.2.4. Table 2, entry 4. Azoxybenzene **16** (65.4 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at 130 °C for 18 h to afford azobenzene **17** (49 mg, 0.27 mmol, 82%) and traces of 1,2-diphenylhydrazine **18**. NMR spectra details as above.

4.3.3. Reduction of azobenzene ***17***

4.3.3.1. Table 3, entry 1. Azobenzene **17** (60.1 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford 1,2-diphenylhydrazine **18** (54.1 mg, 0.29 mmol, 89%). NMR spectra details as above.

4.3.3.2. Table 3, entry 2. Azobenzene **17** (60.1 mg, 0.33 mmol) was treated with DMAP salt **9** (356.6 mg, 0.66 mmol) and sodium hydride (31,7 mg, 1.32 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford 1,2-diphenylhydrazine **18** (54.1 mg, 0.30 mmol, 90%). NMR spectra details as above.

4.3.3.3. Table 3, entry 3. Azobenzene **17** (60.1 mg, 0.33 mmol) was treated with DMAP salt **9** (178.3 mg, 0.33 mmol) and sodium hydride (15.8 mg, 0.66 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h to afford 1,2-diphenylhydrazine **18** (48.0 mg, 0.26 mmol, 79%) and remaining starting material **17** (4.8 mg, 0.026 mmol, 8%). NMR spectra details as above.

4.3.3.4. Table 3, entry 4. Azobenzene **17** (60.1 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at 130 °C for 18 h to afford remaining starting material **17** (7.2 mg, 0.04 mmol, 12%), 1,2-diphenylhydrazine **18** (43.8 mg, 0.24 mmol, 72%) and aniline **19** (2.5 mg, 0.026 mmol, 4%). NMR spectra details as above.

4.3.4. Reduction of hydrazine derivatives ***24–27***

4.3.4.1. Table 4, entry 1. Tetraphenylhydrazine **24** (111.0 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h. The crude product was purified by column chromatography on silica eluting with EtOAc (7%) in hexane to afford diphenylamine **28** as an off-white solid (87.1 mg, 0.51 mmol, 78%). M. Pt. 51–53 °C (lit. 52–54 °C) [8]. δ_H (400 MHz, $CDCl_3$): 6.93 (2H, tt, $J = 7.6$, 0.8 Hz, Ar*H*), 7.09–7.06 (4H, m, Ar*H*), 7.29–7.24 (4H, m, Ar*H*). δ_C (100 MHz, $CDCl_3$): 118.0, 121.2, 129.5, 143.3. IR (NEAT) ν (cm^{-1}) = 689, 743, 877, 1175, 1318, 1495, 1515, 1589, 3382. *m/z* (EI) $C_{12}H_{11}N$ [M]: 169.1.

4.3.4.2. Table 4, entry 2. Tetraphenylhydrazine **24** (111.0 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at 130 °C for 18 h to afford diphenylamine **28** (100.5 mg, 0.59 mmol, 90%) after purification (chromatography on silica using EtOAc (7%) in hexane as eluent). NMR spectra details as above.

4.3.4.3. Table 4, entry 3. 1-(Diphenylamino)piperidin-2-one **25** (54 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at room temperature under UV light for 18 h. The crude product was purified by column chromatography on silica eluting with EtOAc (5%) in hexane to afford diphenylamine **28** (12 mg, 0.071 mmol, 35%). NMR spectra details as above.

4.3.4.4. Table 4, entry 4. 1-(Diphenylamino)piperidin-2-one **25** (54 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at 130 °C for 18 h ^{1}H NMR of the crude product showed traces of diphenylamine **28**. NMR spectra details as above.

4.3.4.5. Table 4, entry 5. 1-(Diphenylamino)piperidine **26** (50 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at room temperature under UV light for 18 h. The crude product was purified by column chromatography on silica using EtOAc (2%) in hexane to afford diphenylamine **28** (6 mg, 0.036 mmol, 18%). NMR spectra details as above.

4.3.4.6. Table 4, entry 6. 1-(Diphenylamino)piperidine **26** (54 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at 130 °C for 18 h ^{1}H NMR of the crude product showed only remaining starting material (47 mg, 0.17 mmol, 94%).

4.3.4.7. Table 4, entry 7. 1-(diphenylamino)piperidin-2-one **25** (54 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at room temperature under UV light for 36 h. The crude product was purified by column chromatography on silica using EtOAc (5%) in hexane to afford diphenylamine **28** (14 mg, 0.083 mmol, 40%). NMR spectra details as above.

4.3.4.8. Table 4, entry 8. 1-(diphenylamino)piperidine **26** (50 mg, 0.20 mmol) was treated with DMAP salt **9** (324 mg, 0.60 mmol) and sodium hydride (29 mg, 1.20 mmol) in dry DMF (3 mL) at room temperature under UV light for 36 h. The crude product was purified by column chromatography on silica using EtOAc (2%) in hexane to afford diphenylamine **28** (7.7 mg, 0.045 mmol, 23%). NMR spectra details as above.

4.3.4.9. Table 4, entry 9. 1-(Diphenylamino)piperidin-2-one **25** (54 mg, 0.20 mmol) was treated with DMAP salt **9** (648 mg, 1.20 mmol) and sodium hydride (58 mg, 2.40 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h. The crude product was purified by column chromatography on silica using EtOAc (5%) in hexane to afford diphenylamine **28** (12.3 mg, 0.073 mmol, 36%). NMR spectra details as above.

4.3.4.10. Table 4, entry 10. 1-(Diphenylamino)piperidine **26** (50 mg, 0.20 mmol) was treated with DMAP salt **9** (648 mg, 1.20 mmol) and sodium hydride (58 mg, 2.40 mmol) in dry DMF (5 mL) at room

temperature under UV light for 18 h. The crude product was purified by column chromatography on silica using EtOAc (2%) in hexane to afford diphenylamine **28** (7 mg, 0.042 mmol, 21%). NMR spectra details as above.

4.3.4.11. Table 4, entry 11. Bipiperidine **27** (55.5 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at room temperature under UV light for 18 h ^{1}H NMR of the crude reaction mixture showed only remaining starting material (38.9 mg, 0.23 mmol, 70%), yield was quantified by use of 1,3,5-trimethoxybenzene as an internal NMR standard.

4.3.4.12. Table 4, entry 12. Bipiperidine **27** (55.5 mg, 0.33 mmol) was treated with DMAP salt **9** (540.2 mg, 1.0 mmol) and sodium hydride (48.0 mg, 2.0 mmol) in dry DMF (5 mL) at 130 °C for 18 h ^{1}H NMR of the crude product showed only remaining starting material (38.9 mg, 0.23 mmol, 70%), yield was quantified by use of 1,3,5-trimethoxybenzene as an internal standard.

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References

[1] C. Yu, B. Liu, L. Hu, J. Org. Chem. 66 (2001) 919–924.
[2] (a) F.A. Khan, J. Dash, C. Sudheer, R.K. Gupta, Tetrahedron Lett. 44 (2003) 7783–7787;
(b) R.M. Deshpande, A.N. Mahajan, M.M. Diwakar, P.S. Ozarde, R.V. Chaudhari, J. Org. Chem. 69 (2004) 4835–4838;
(c) P.M.G. Bavin, Org. Synth. 40 (1960) 5;
(d) J. Souppe, L. Danon, J.L. Namy, H.B. Kagan, J. Organomet. Chem. 250 (1983) 227–236;
(f) N. Sakai, K. Fujii, S. Nabeshima, R. Ikeda, T. Konakahara, Chem. Commun. 46 (2010) 3173–3175;
(g) N. Sakai, S. Asama, S. Anai, T. Konakahara, Tetrahedron 70 (2014) 2027–2033;
(h) L. Hu, X. Cao, L. Chen, et al., Chem. Commun. 48 (2012) 3445–3447;
(i) M.L. Di Gioia, A. Leggio, I.F. Guarino, V. Leotta, E. Romio, A. Liguori, Tetrahedron Lett. 56 (2015) 5341–5344;
(j) R. Porta, A. Puglisi, G. Colombo, S. Rossi, M. Benaglia, Beilstein. J. Org. Chem. 12 (2016) 2614–2619.
[3] (a) J.A. Murphy, T.A. Khan, S.-Z. Zhou, D.W. Thomson, M. Mahesh, Angew. Chem. Int. Ed. 44 (2005) 1356–1360;
(b) J.A. Murphy, S.-Z. Zhou, D.W. Thomson, et al., Angew. Chem. Int. Ed. 46 (2007) 5178–5183;
(c) J.A. Murphy, F. Schoenebeck, S.-Z. Zhou, Y. Uenoyama, Y. Miclo, T. Tuttle, J. Am. Chem. Soc. 129 (2007) 13368–13369;
(d) J.A. Murphy, J. Garnier, S.R. Park, F. Schoenebeck, S.-Z. Zhou, A.T. Turner, Org. Lett. 10 (2008) 1227–1230;
(e) J. Garnier, J.A. Murphy, S.Z. Zhou, A.T. Turner, Synlett (2008) 2127–2131;
(f) S.P.Y. Cutulic, J.A. Murphy, H. Farwaha, S.-Z. Zhou, E. Chrystal, Synlett (2008) 2132–2136;
(g) J.A. Murphy, F. Schoenebeck, N.J. Findlay, D.W. Thomson, S.-Z. Zhou, J. Garnier, J. Am. Chem. Soc. 131 (2009) 6475–6479;
(h) P.I. Jolly, S. Zhou, D.W. Thomson, et al., Chem. Sci. 3 (2012) 1675–1679;
(i) E. Cahard, F. Schoenebeck, J. Garnier, S.P.Y. Cutulic, S. Zhou, J.A. Murphy, Angew. Chem. Int. Ed. 51 (2012) 3673–3676;
(j) E. Doni, S. O'Sullivan, J.A. Murphy, Angew. Chem. Int. Ed. 52 (2013) 2239–2242;
(k) E. Doni, B. Mondal, S. O'Sullivan, T. Tuttle, J.A. Murphy, J. Am. Chem. Soc. 135 (2013) 10934–10937;
(l) S. Zhou, G.M. Anderson, B. Mondal, et al., Chem. Sci. 5 (2014) 476–482;
(m) S. O'Sullivan, E. Doni, T. Tuttle, J.A. Murphy, Angew. Chem. Int. Ed. 53 (2014) 474–478;
(n) J.A. Murphy, J. Org. Chem. 79 (2014) 3731–3746;
(o) S. Zhou, E. Doni, G.M. Anderson, et al., J. Am. Chem. Soc. 136 (2014) 17818–17826;
(p) E. Doni, J.A. Murphy, Org. Chem. Front. 1 (2014) 1072–1076;
(q) S.S. Hanson, E. Doni, K.T. Traboulsee, G. Coulthard, J.A. Murphy, C.A. Dyker, Angew. Chem. Int. Ed. 54 (2015) 11236–11239;
(r) S.S. Hanson, N.A. Richard, C.A. Dyker, Chem. Eur. J. 21 (2015) 8052–8055;
(s) J.P. Barham, G. Coulthard, R.G. Kane, N. Delgado, M.P. John, J.A. Murphy, Angew. Chem. Int. Ed. 55 (2016) 4492–4496;
(t) J.P. Barham, G. Coulthard, K. Emery, et al., J. Am. Chem. Soc. 138 (2016) 7402–7410.
[4] (a) M. Brasholz, Angew. Chem. Int. Ed. 56 (2017) 10280–10281;
(b) I. Ghosh, R.S. Shaikh, B. Koenig, Angew. Chem. Int. Ed. 56 (2017) 8544–8549;
(c) W. Liu, X. Yang, Y. Gao, C.-J. Li, J. Am. Chem. Soc. 139 (2017) 8621–8627;
(d) L. Zhang, L. Jao, J. Am. Chem. Soc. 139 (2017) 607–610;
(e) H. Yang, L. Zhang, L. Jiao, Chem. Eur. J. 23 (2017) 65–69;
(f) L. Zhang, H. Yang, L. Jiao, J. Am. Chem. Soc. 138 (2016) 7151–7160;
(g) J. Broggi, M. Rollet, J.-L. Clement, et al., Angew. Chem. Int. Ed. 55 (2016) 5994–5999;
(h) M. Patil, J. Org. Chem. 81 (2016) 632–639;
(i) G.M. Anderson, I. Cameron, J.A. Murphy, T. Tuttle, RSC. Adv. 6 (2016) 11335–11343.
[5] B.M. Hofmann, D. Lukoyanov, Z.-Y. Yang, D.R. Dean, L.C. Seefeldt, Chem. Rev. 114 (2014) 4041–4062.
[6] (a) T. Kajimoto, H. Takahashi, J. Tsuji, Bull. Chem. Soc. Jpn. 55 (1982) 3673–3674;
(b) J. Fotie, J.L. Rhodus, H.A. Taha, C.S. Reid, Heteroat. Chem. 23 (2012) 598–604.
[7] U. Svanholm, V.D. Parker, J. Am. Chem. Soc. 94 (1972) 5507–5508.
[8] Y. Zhang, Q. Tang, M. Luo, Org. Biomol. Chem. 9 (2011) 4977–4982.
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