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Amine Photocyanation

A Highly Active System for the Metal-Free Aerobic Photocyanation of Tertiary Amines with Visible Light: Application to the Synthesis of Tetraponerines and Crispine A

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Abstract: A highly efficient metal-free catalytic system for the aerobic photocyanation of tertiary amines with visible light is reported. The use of air as terminal oxidant offers an improved safety profile compared with pure oxygen, the used compact fluorescent lamp (CFL) light sources are highly economical, and no halogenated solvents are required. This system not only proves to be effective for a wide variety of trialkylamines, pharmaceuticals, and alkaloids but remarkably also allows the lowest catalyst loading (0.00001 mol% or 0.1 ppm) ever reported for an organic dye. Bruylants reactions and C-alkylation/decyanations were performed on the obtained α-aminonitriles to demonstrate the postfunctionalization of complex molecules. The catalytic system is furthermore applied in the short and effective syntheses of the alkaloids (±)-crispine A and the tetraponerines T7 and T8.

Introduction

In recent years, visible-light photoredox catalysis has emerged as a versatile tool for developing new synthetic methodologies. The most extensively studied and widely used photocatalysts are complexes of ruthenium and iridium with bidentate N,N- and C,N-ligands, which have, for example, been employed in C–C, C–N, C–O, and C–P bond formations.[1] Nevertheless, inexpensive and metal-free organic dyes (eosin Y, methylene blue, rose bengal, etc.) have also been successfully applied in photoredox reactions and represent an attractive, cost-effective alternative to the, in part, very expensive transition-metal catalysts.[2]

α-Aminonitriles represent an important class of compounds—their numerous modes of reactivity make them chameleonic and widely applicable intermediates in organic chemistry.[3] For more than a century, their synthesis was essentially restricted to the well-known Strecker reaction.[4] An alternative route was presented by Murahashi et al. who reported a direct oxidative cyanation of amines[5] and similar sp^3 C–H activations for the synthesis of α-aminonitriles have since been developed.[6] In addition to different catalytic[6b,7] and stoichiometric approaches,[8] visible-light photoredox catalysis is a particularly promising technique in this respect. By using visible-light irradiation, Rueping and co-workers reported the α-cyanation of activated tertiary amines using KCN and $[Ir(ppy)_2bpy]PF_6$ (ppy = 2-phenylpyridine, bpy = 2,2′-bipyridine) as a photocatalyst.[9] Stephenson's group obtained 2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile in a two-step synthesis employing $[Ru(bpy)_3Cl_2]$ and $BrCCl_3$ as the terminal oxidant.[10] In terms of organic photocatalysis, eosin Y was employed by König and Hari for the oxidative generation of 2-aryl-1,2,3,4-tetrahydroisoquinoline-1-carbonitriles.[11] In addition, Tan et al. developed a catalytic system using rose bengal (5 mol%), graphene oxide, and TMSCN for the synthesis of the same type of aminonitriles.[12] To overcome the long reaction times associated with these procedures, continuous-flow photoredox applications are an interesting alternative. Seeberger and co-workers reported the continuous-flow oxidative cyanation of primary and secondary amines catalyzed by singlet oxygen ($^1O_2$, generated by 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (TPP) in CH_2Cl_2).[13] Rueping's group also reported a continuous-flow method using rose bengal (5 mol%) and TMSCN for the photocyanation of different *N*-aryl-tetrahydroisoquinolines.[14]

Unfortunately, most of these methodologies have a rather narrow substrate scope and are restricted to *N*-aryl- or *N*-benzylamines, or even to the small group of *N*-substituted tetrahydroisoquinolines. In contrast, tertiary aliphatic amines have mainly been used in photoredox reactions as sacrificial electron donors so far.[1c] With respect to the photocyanation of natural products, Khuong-Huu et al. functionalized the alkaloids vincadifformine and tabersonine by using KCN in combination with methylene blue or rose bengal (with the photo"catalyst" being used in equimolar quantity).[15] Later, the same

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group reported the α-cyanation of sparteine, lupanine, and its derivatives sensitized by eosin Y or methylene blue (10 wt% or equimolar quantity).[16] Other photocatalysts employed for the cyanation of alkaloids include 9,10-dicyanoanthracene, *N*,*N*′-dimethyl-2,7-diazapyrenium-bis-(tetrafluoroborate) ($DAP^{2+}\cdot 2BF_4^-$),[17] and TPP.[18] Recently, Stephenson and Beatty described a fragmentation/α-cyanation of (+)-catharanthine in the presence of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ ($dF(CF_3)ppy$ = 2-(2,4-difluorophenyl)-5-trifluoromethylpyridine, dtbbpy = 4,4′-di-*tert*-butyl-2,2′-biyridine) and TMSCN[19] whereas Tan et al. reported the cyanation of (*S*)-nicotine and *N*,*N*-dimethyl-1-phenylethan-1-amine in appreciable yields by using rose bengal (5 mol%) but long reaction times (up to 48 h) and the expensive graphene oxide as terminal oxidant were required.[12]

We were surprised by the lack of a more economical and efficient procedure as well as the lack of applications of photogenerated α-aminonitriles in total synthesis and the postfunctionalization of natural products. Herein, we describe the use of the inexpensive dye rose bengal in combination with air and TMSCN as a highly active catalytic system for the α-photocyanation of tertiary aliphatic amines. This system not only proves effective for a wide variety of amine substrates but remarkably permits the reduction of the catalyst loading down to 0.00001 mol% (=0.1 ppm!), the lowest value ever reported for an organic dye. The use of air instead of pure oxygen is advantageous in terms of safety, no halogenated solvents are required, and the used compact fluorescent lamp (CFL) light sources are highly economical.[20] A variety of derivatization reactions were performed on the synthesized α-aminonitriles, demonstrating their versatility as building blocks. Finally, the application of the catalytic system to novel, short and efficient syntheses of the alkaloids tetraponerine T7 and T8 as well as (±)-crispine A is demonstrated.

Results and Discussion

During the last decade, our research group has been taking advantage of the chemistry of α-aminonitriles in the synthesis of various nitrogen-containing natural products and other N-heterocycles.[21] Based on our experience with α-aminonitrile chemistry and encouraged by the lack of efficient photocyanations of tertiary aliphatic amines, we explored this type of sp^3 C–H activation in view of its potential application to the total synthesis of natural products. Tri-*n*-butylamine (**1a**) was chosen as a reference substrate in combination with air and TMSCN as the cyanide source using a standard 24 W household fluorescent bulb. Reaction times and yields were determined for a series of potential photocatalysts employed (Figure 1), the results are summarized in Table 1.

The formation of the product was observed in all cases. However, the best results were obtained with rose bengal (3 h, 90%, entry 7), which was selected as the photocatalyst for the cyanations. Attempts to reduce the volume of solvent or the amount of

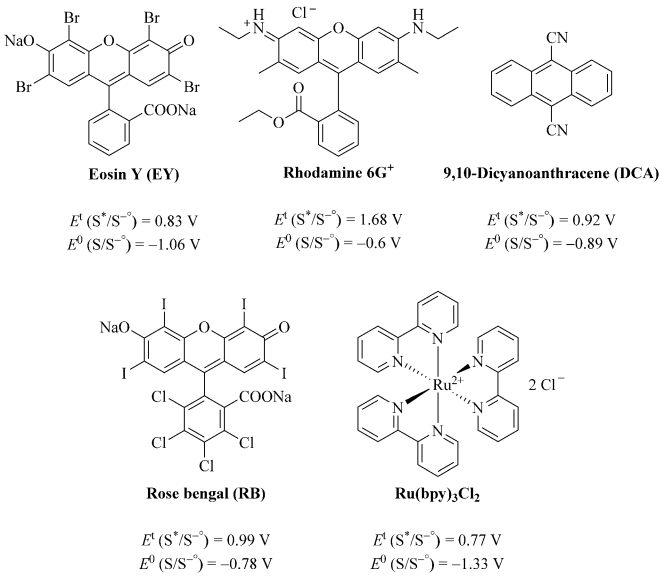
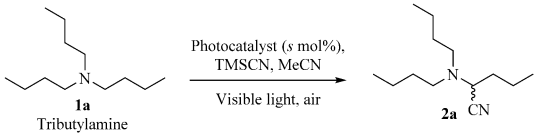


Figure 1. Photocatalysts and their redox potentials (S = sensitizer) in MeCN versus saturated calomel electrode (SCE) or normal hydrogen electrode $(NHE)^{+\cdot}$.[2b,22]

TMSCN initially led to unsatisfactory results (entry 8). Nevertheless, an excellent outcome (98% yield by NMR spectroscopy) was seen when the volume of solvent was reduced to 2.0 mL and 4.0 equivalents of TMSCN were used (entry 9). When the reaction was run under an air atmosphere instead of bubbling air through the mixture, the yield decreased considerably

Table 1. Screening of catalysts and reaction conditions.[a]



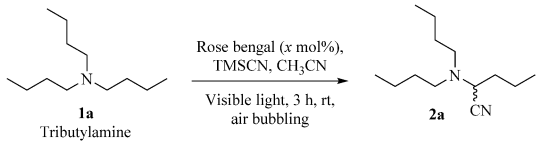
	Catalyst	Solvent volume [mL]	TMSCN [equiv]	Reaction time [h]	Yield [%][b]
1	Eosin Y (1 mol%)	5.0	4.0	15	quant.
2	Rhodamine 6G (1 mol%)	5.0	4.0	15	72
3[c]	DCA (1 mol%)	5.0	4.0	15	42
4	Rose bengal (1 mol%)	5.0	4.0	15	quant.
5	$[Ru(bpy)_3Cl_2]\cdot 6H_2O$ (1 mol%)	5.0	4.0	15	57
6	Eosin Y (1 mol%)	5.0	4.0	3	79
7	Rose bengal (1 mol%)	5.0	4.0	3	90
8	Rose bengal (1 mol%)	2.0	2.0	2	59
9	Rose bengal (1 mol%)	2.0	4.0	3	98
10[d]	Rose bengal (1 mol%)	2.0	4.0	3	49
11[e]	Rose bengal (1 mol%)	2.0	4.0	3	10
12	Rose bengal (1 mol%)	2.5[f]	4.0 (KCN)	3	64
13[g]	Rose bengal (1 mol%)	2.0	4.0	24	5
14	–	2.0	4.0	3	11
15	–	2.0	4.0	6	38
16	Rose bengal (0.5 mol%)	2.0	4.0	3	90

[a] Reaction conditions: 210 μmol of tributylamine (1.0 equiv) were used. The reaction mixture was stirred and irradiated with a 24 W fluorescent household bulb at room temperature under air bubbling. [b] Determined by ^1H NMR spectroscopy by using CH_2Br_2 as an internal standard. [c] UV light (λ = 300–400 nm). [d] Air atmosphere, no bubbling. [e] Nitrogen bubbling. [f] 2.0 mL MeCN + 0.5 mL D_2O. [g] No irradiation.

(entry 10), which is in agreement with the very low yield obtained under a nitrogen atmosphere (entry 11), proving oxygen to be essential for the photocyanation. Control experiments in the absence of light (entry 13) or catalyst (entries 14 and 15) demonstrated that the combination of light and rose bengal is required for an appreciable reaction rate although an uncatalyzed background reaction takes place. Other cyanating agents such as KCN also produced α-aminonitrile **2a** (entry 12) but the yield was significantly lower than with TMSCN (entry 9). Reduction of the catalyst loading to 0.5 mol% still afforded a 90% yield after only 3 h (entry 16), indicating that even lower catalyst loadings might still be effective.

Remarkably, loadings of 0.1 mol% (Table 2, entry 2) and 0.01 mol% (entry 3) still afforded good to excellent yields. With 0.001 mol% (entry 4) and 0.0001 mol% (entry 5) of rose bengal, the reaction continued affording acceptable results

Table 2. Reduction of catalyst loading.[a]



	Rose bengal [mol%]	Average yield [%][b]	TON[c]	TOF [h^{-1}][d]
1	1	97.3 ± 0.3	85.9 ± 0.4	28.6 ± 0.1
2	0.1	86.2 ± 0.6	748 ± 7	249 ± 2
3	0.01	69.0 ± 1.6	5760 ± 17	1920 ± 6
4	0.001	45.6 ± 0.7	34 267 ± 80	11 422 ± 27
5	0.0001	24.7 ± 1.0	133 333 ± 1100	44 444 ± 367
6	0.00001	21.7 ± 2.3	1 030 000 ± 240 000	343 333 ± 80 000
7	–	11.4 ± 0.1	–	–

[a] Reaction conditions: 210 μmol of tributylamine (1.0 equiv), TMSCN (4.0 equiv), and 2.0 mL of MeCN were used. The reaction mixture was stirred and irradiated under air bubbling with a 24 W fluorescent household bulb for 3 h at room temperature. Each reaction was run at least in triplicate (see the Supporting Information, page S4). [b] Determined by ^{1}H NMR spectroscopy by using CH_2Br_2 as an internal standard. [c] TON = *n*(product)/*n*(rose bengal) after subtraction of background reaction (Table 1, entry 7). [d] TOF = (*n*(product)/*n*(rose bengal))/3 h after subtraction of background reaction (Table 1, entry 7).

with yields between 25–45% after 3 h. A catalyst loading of 0.0001 mol% (10 ppm, entry 5) already corresponds to the lowest value ever reported for an organic dye, which gave a turnover number (TON) in excess of 130 000. The limit of the catalyst was reached at 0.00001 mol% or 0.1 ppm (entry 6, TON > 1 000 000). In this case, the yield dropped to 21.7%, but was still twofold higher than the yield of the uncatalyzed background reaction. Full absorption at λ_{max} of rose bengal (562 nm) occurs in entries 1–3 as judged by UV/VIS spectroscopy and could explain the lower TON and turnover frequency (TOF) values at these three catalyst loadings.

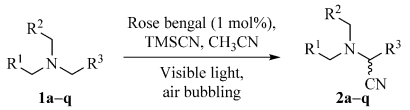
To prove that UV emissions from the CFL lamp play no major role in the photocyanation, UV exclusion experiments were performed at 0.1 mol% catalyst loading. Only a moderate decrease in the yield could be observed when the reaction vessel was either irradiated through a UV glass filter (390 nm cutoff) or a solution of benzophenone in ethanol (0.5 M, path length 14 mm, see the Supporting Information, page S5).

After optimization of the reaction conditions, the scope and limitations of the procedure were investigated by using different tertiary aliphatic amines (Table 3). Good to excellent yields were observed in most cases, illustrating the efficiency of the developed photocyanation method. Longer reaction times were required for *N*,*N*-dimethylalkylamines (entries 4 and 6). This behavior could be explained by the oxidation potentials of tertiary amines, which decrease with increasing chain length (e.g., Me_3N, +0.82 V; Et_3N, +0.79 V; nBu_3N, +0.62 V; measured vs SCE).[23] Remarkably, high regioselectivities were observed when different α-protons were available for substitution (entries 4–8, 10 and 11). In most cases, the reaction took place at the less hindered carbon; however, electronic effects also seem to play an important role.[23] When triethanolamine (**1i**) was subjected to the photocyanation, the OH groups in the corresponding α-aminonitrile were silylated (entry 9). To increase the molecular complexity of the substrates, we decided to investigate the photocyanation of (−)-nicotine (**1l**), (+)-sparteine (**1m**), orphenadrine (**1n**), atropine (**1o**), gramine (**1p**), and strychnine (**1q**, entries 12–17). As anticipated, similar results were encountered. However, no reaction was observed for quinine (**1r**), DABCO (1,4-diazabicyclo[2.2.2]octane; **1s**), and hexamethylenetetramine (**1t**, entries 18–20). A potential explanation could be the violation of Bredt's rule in the formation of bridgehead iminium ions. On the other hand, DABCO is well known to act as an excellent charge-transfer quencher, in particular for singlet oxygen.[24] The same behavior has been reported for *Cinchona* alkaloids such as quinine (**1r**).[25] To explore the roles of quenchers in the reaction, inhibitor and light–dark cycle experiments were performed to check the potential involvement of singlet oxygen ($^1O_2$), radical chain reactions, or light-independent processes in the photocyanation (see the Supporting Information, pages S51–S53). However, no clear mechanistic conclusions could be drawn from the results.

To demonstrate the application of photogenerated α-aminonitriles in the synthesis of new compounds and natural products, 2-(dipropylamino)butanenitrile (**2b**) and 5-cyanonicotine (**2l**) were selected as exemplary candidates for further derivatization. First, a one-pot C-alkylation/reductive decyanation was attempted. The α-aminonitriles were deprotonated with lithium diisopropylamide (LDA) at −78 °C and alkylated with 1-iodoheptane. In situ reduction of the alkylation product with $NaCNBH_3$ afforded the heptyl-substituted compounds **3a** and **3b** in 77% and 44% yield, respectively (Scheme 1). Using another well-known reactivity mode of α-aminonitriles, compounds **2b** and **2l** were subjected to a Bruylants reaction with *n*-pentylmagnesium bromide in THF at −20 °C, furnishing the pentyl-substituted compounds **4a** and **4b** in 64% and 45% yield, respectively (Scheme 1). These examples underline the synthetic potential of photocatalytic postfunctionalizations of amines and alkaloids.

Furthermore, the direct application of photogenerated α-aminonitriles in the synthesis of (±)-crispine A as well as an enantioselective approach to tetraponerines T7 and T8 could

Table 3. Scope of the photocyanation.[a]



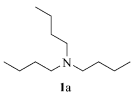
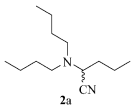
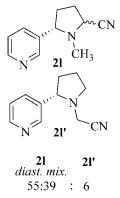
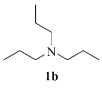
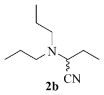
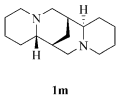
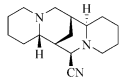
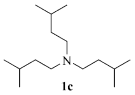
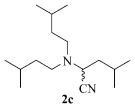
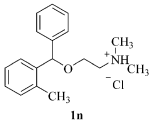
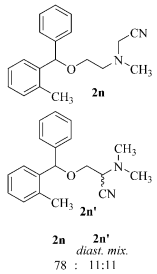
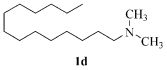
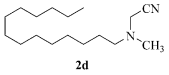
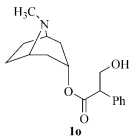
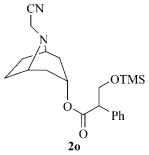
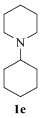
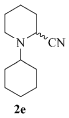
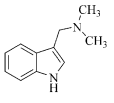
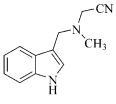
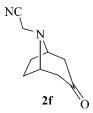
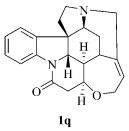
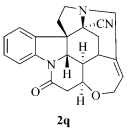
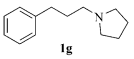
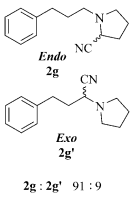
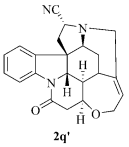
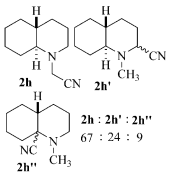
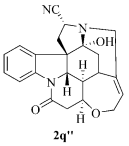
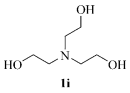
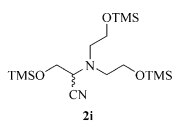
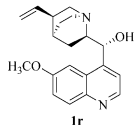
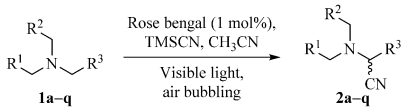
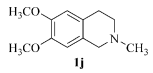
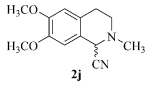
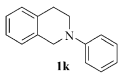
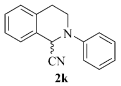
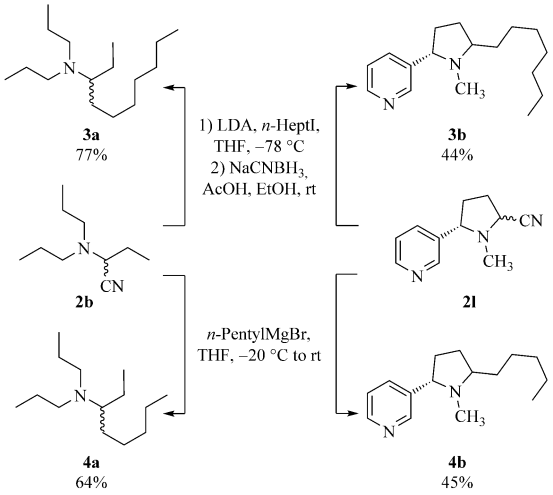
	Tertiary amine	Time [h]	Product	Yield [%][b]		Tertiary amine	Time [h]	Product	Yield [%][b]
1	 1a	3.0	 2a	89	12[c]	 1l	3.0	 2l / 2l' diast. mix. 55:39 : 6	89
2[c]	 1b	3.0	 2b	74	13	 1m	3.0	 2m	52
3	 1c	3.5	 2c	84	14[c,d]	 1n	24.0	 2n / 2n' diast. mix. 78 : 11:11	74
4	 1d	18.0	 2d	80	15	 1o	16.0	 2o	65
5	 1e	3.0	 2e	74	16	 1p	15.0	 2p	20
6	 1f	24.0	 2f	61	17[e]	 1q	48.0	 2q	11
7[d]	 1g	3.0	 Endo 2g / Exo 2g' 2g : 2g' 91 : 9	68				 2q'	22
8[d]	 1h	4.0	 2h / 2h' / 2h'' 2h : 2h' : 2h'' 67 : 24 : 9	82				 2q''	5
9	 1i	5.0	 2i	37	18[f]	 1r	24.0	–	–

Table 3. (Continued)

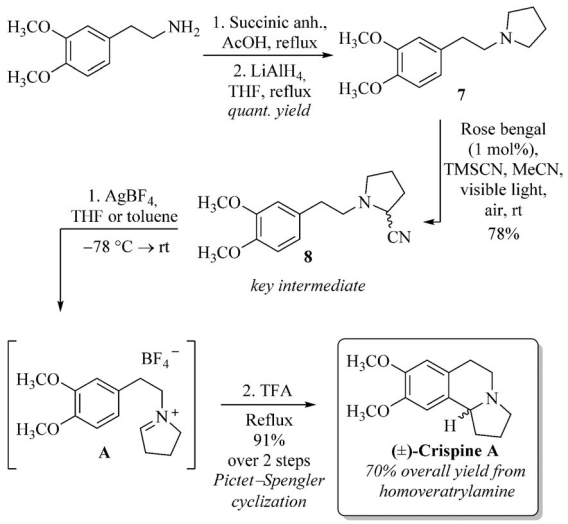


	Tertiary amine	Time [h]	Product	Yield [%][b]		Tertiary amine	Time [h]	Product	Yield [%][b]
10	 1j	3.0	 2j	80	19[f]	 1s	24.0	–	–
11	 1k	3.0	 2k	80	20[f]	 1t	24.0	–	–

[a] Reaction conditions: amine (1.00 mmol, 1.0 equiv), rose bengal (10.0 μmol, 1 mol%), TMSCN (4.00 mmol, 4.0 equiv), and 8.0 mL of MeCN. The reaction mixture was stirred and irradiated under air bubbling with a 24 W fluorescent household bulb at room temperature. [b] Isolated yield. [c] The reaction was also performed on the gram scale (see the Supporting Information). [d] Ratio determined by ^{1}H NMR spectroscopy. [e] The reaction was performed in a mixture of CH_3CN and $CHCl_3$ (1:1) with 2 mol% of rose bengal. Products were separated by preparative HPLC. [f] No product was detected. Starting material was completely recovered.



Scheme 1. One-pot C-alkylation/reductive decyanation and Bruylants reaction of α-aminonitriles **2b** and **2l**.

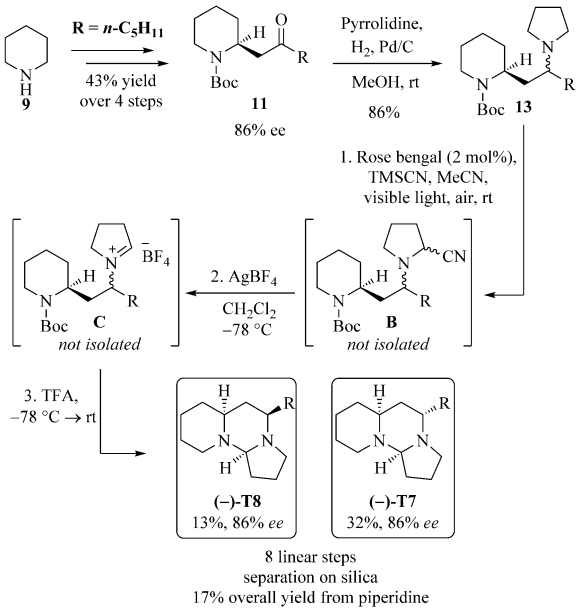


Scheme 2. Synthesis of (±)-crispine A.

be demonstrated. Crispine A is a tricyclic tetrahydroisoquinoline alkaloid isolated from the welted thistle, *Carduus crispus*.[26] It can be prepared by a Pictet–Spengler cyclization of an iminium ion obtained from the corresponding α-aminonitrile (Scheme 2). Our synthesis started with the preparation of pyrrolidine **7** from commercial homoveratrylamine (**5**) in a two-step procedure with quantitative yield. Photocyanation with the rose bengal/TSMCN/air system under standard conditions furnished α-aminonitrile **8** in 78% yield. In situ generation of iminium ion **9** with $AgBF_4$ followed by addition of trifluoroacetic acid (TFA) as co-solvent (surprisingly required to effect cyclization although iminium salt **A** is stable and does not form the enamine in the absence of base) afforded (±)-crispine A in 91% yield over two steps. Thus, the overall yield of the natural product amounted to 70%. This route represents one of the shortest (four linear steps) and highest yielding syntheses of crispine A.

Another synthetic application of the photocyanation is illustrated by the synthesis of tetraponerines T7 and T8. The tetraponerines T1–T8 (see the Supporting Information, page S53) represent a class of tricyclic alkaloids sharing an aminal structure. These compounds have been isolated from the poison of ants of the genus *Tetraponera* (*Pseudomyrmecinae*), which is known to cause the paralysis and death of their enemies, presumably by inhibition of nicotinic acetylcholine receptors.[27] The tricyclic skeleton should be easily assembled by generating an appropriate α-aminonitrile intermediate (Scheme 3).

The reaction route started with the enantioselective organocatalytic synthesis of the key precursor **11**, which was prepared in 43% yield over four steps from piperidine **9** in an L-proline-

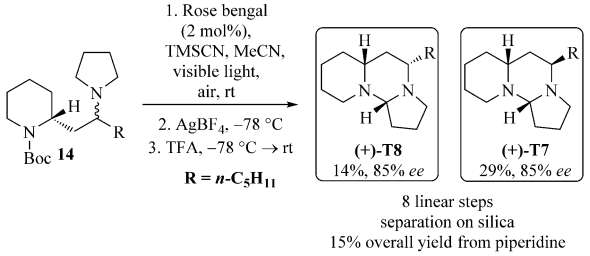


Scheme 3. Synthesis of tetraponerines (−)-T7 and (−)-T8.

catalyzed Mannich reaction. The *S*-enantiomer was obtained in 86% *ee*, which could be increased further at the expense of the yield by lowering the reaction temperature (see the Supporting Information, page S54). Reductive amination with pyrrolidine in the presence of Pd/C and H_2 provided amine **13** (as a diastereomeric mixture) in 86% yield. A one-pot procedure consisting of the chemoselective photocyanation of the pyrrolidine moiety to α-aminonitrile **B**, subsequent generation of iminium ion **C** with $AgBF_4$, and N-deprotection with TFA afforded a mixture of tetraponerines (−)-T7 and (−)-T8. Flash chromatography permitted the separation of tetraponerines (−)-T7 and (−)-T8, which were obtained in 32% and 13% yield, respectively.

By using D-proline in the Mannich reaction, the enantiomeric tetraponerines (+)-T7 and (+)-T8 were obtained likewise in a 15% overall yield (Scheme 4). This procedure can likely be extended to the stereoselective total synthesis of the tetraponerines T3 and T4 by using 2-pentanone instead of 2-heptanone in the Mannich reaction.

The examples presented above not only illustrate new routes for the successful synthesis of (±)-crispine A and tetraponerines T8 and T7, but also demonstrate the potential of our photocyanation method as a valuable tool in the total synthesis of natural products.



Scheme 4. Synthesis of (+)-T7, (+)-T8 following the same reaction pathway.

Conclusion

An economic and highly active catalytic system for the metal-free visible-light aerial photocyanation of tertiary aliphatic amines was developed. Short reaction times can conveniently be achieved with a catalyst loading of 1 mol%, but even at loadings as low as 0.1 ppm the photoredox catalysis proceeds significantly faster than the background reaction. A variety of synthetically useful α-aminonitriles were prepared and their utility for postfunctionalization procedures was showcased for nicotine and tri-*n*-propylamine. Moreover, novel, short, and efficient syntheses for the alkaloids (±)-crispine A and the tetraponerines T7 and T8 (both enantiomers) involving the aerial photocyanation were developed.

Experimental Section

General procedure for the photocyanation of tertiary aliphatic amines

A solution of trialkylamine (**1a–q**, 1.0 equiv), rose bengal (1.0 mol%), and TMSCN (4.0 equiv) in CH_3CN (8 mL mmol^{-1}) was irradiated under air bubbling with a 24 W fluorescent household bulb at room temperature. Upon completion (monitored by TLC), a concentrated aqueous solution of K_2CO_3 was added and allowed to stir for an additional 10 min. The reaction mixture was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the crude product was passed through a plug of aluminum oxide (basic) using CH_2Cl_2 as the eluent. In most cases, the product was used without further purification. In some cases, an additional purification step (flash chromatography) was required.

Rose bengal: studies on the catalyst loading

Rose bengal stock solutions: In a 25 mL volumetric flask, a solution of rose bengal (11.611 mg) in CH_3CN was prepared, generating a general stock solution of 456.4 μM. Three further stock solutions of 220 μM, 7.0 μM, and 224 nM were obtained by dilution of the former solution. For the loading experiments, tri-*n*-butylamine (**1a**, 210 μmol, 1.0 equiv) and different amounts of catalyst (0.1, 0.01, 0.001, 0.0001, and 0.00001 mol% using the above-mentioned stock solutions) were brought to a final volume of 2 mL of CH_3CN, followed by addition of TMSCN (4.0 equiv). The mixtures were stirred and irradiated under air bubbling with a 24 W fluorescent household bulb (ca. 8 cm distance to reaction vessel) at room temperature for 3 h. The solvent was removed under reduced pressure and a defined amount of CH_2Br_2 (NMR internal standard) was added. The mixture was dissolved in $CDCl_3$ and the ^1H NMR spectrum was measured; the yield of the reaction was determined by integration of the internal standard and the product signals.

All other procedures, materials, and methods as well as compound characterization data including 1D and 2D NMR spectra, HPLC traces, along with additional results can be found in the Supporting Information.

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Keywords: alkaloids · amines · aminonitriles · photocatalysis · total synthesis

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