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Iron-catalyzed reductive strecker reaction

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ABSTRACT

Strecker reaction is widely applied for the synthesis of amino acids from aldehydes, amines and cyanides. Herein, we report the FeI_2-catalyzed reductive Strecker type reaction of formamides instead of aldehydes to produce amino acetonitriles. The challenging capture of carbinolamine intermediates by CN^- was achieved *via* Fe catalysis. This approach afforded better yields than the use of Ir- or Rh-catalysts. The application ability of this methodology is demonstrated by **1)** one-pot construction of (^{13}C labeled) complex molecules from CO_2 *via* amino acetonitrile intermediates and **2)** convenient production of homologated carboxylic acids from aldehydes.

1. Introduction

The Strecker reaction is a well-known practical synthetic method for α-aminonitriles, widely used for the preparation of amino acids [1]. The classical Strecker reaction described by the German chemist Adolph Strecker (1822–1871) in 1850, and makes use of aldehydes, amines and hydrogen cyanide as starting materials (Fig. 1a) [2]. Notably, the reaction of formaldehyde with ammonia and cyanide to form amino acids is believed to be the essence of the origin of life [3]. Alternatively and unprecedentedly, substitution of formaldehyde reactant with formamides instead in the presence of reductants, Strecker-type products amino-acetonitriles (AANs) could be generated (Fig. 1b). The challenge is how to rationally design the catalyst and suppress the over-reduction of the active iminium/carbinolamine intermediates.

Aminoacetonitrile is used as the key intermediate to many herbicide and pharmaceuticals. Molecules with at least two functional groups are highly valuable and generally used for diverse syntheses of polymeric materials and bio-active products [4]. Accordingly, AANs are recognized as versatile intermediates in organic synthesis, and can readily be transformed into numerous valuable products such as amino acids, α-amino alcohols, α-amino carbonyl compounds, nitrogen containing thiadiazoles and imidazoles heterocycles [5]. Besides, AANs can easily form carbanion species through C-H deprotonation to give the key intermediate formaldehyde iminium ion with cyanomethyl group regarded as the amine protecting group [6]. Hence, AANs are amenable to further transformation with their structural motif prevalent in an array of transformation with their structural motif prevalent in an array of natural products, pharmaceuticals and drug candidates such as Balicatib, Luliconazole, Girgensohnine (Fig. 1c) [7]. As a consequence, selective construction of amino acetonitriles has received considerable attention in recent years.

Other than the traditional methods *via* substitution reaction of organic halides, transition-metal-catalyzed direct cyanation of C-H bonds by oxidative cross dehydrogenative coupling methods has emerged as an attractive approach to AANs derivatives [8]. Notable reported examples feature metal-based catalysts such as Ru [9], Fe [10], V [11], Au [12], Mo [13] and metal-organic frameworks [14], in the presence of oxidants O_2, H_2O_2, or TBHP. Furthermore, AANs derivatives have also recently been obtained under photochemical conditions [15]. However, these procedures involve excess use of oxidants and often have problems of limited chemo-selectivity and functional-group tolerance.

Straightforward procedures to prepare AANs derivatives using readily available and more stable starting materials are highly desirable. Recent progress in the reductive cyanation of amides into AANs derivatives has been demonstrated as ideal pathway albeit challenging [16]. Sato group [17] and Huang group [18] have developed cyanations of tertiary amides employing stoichiometric

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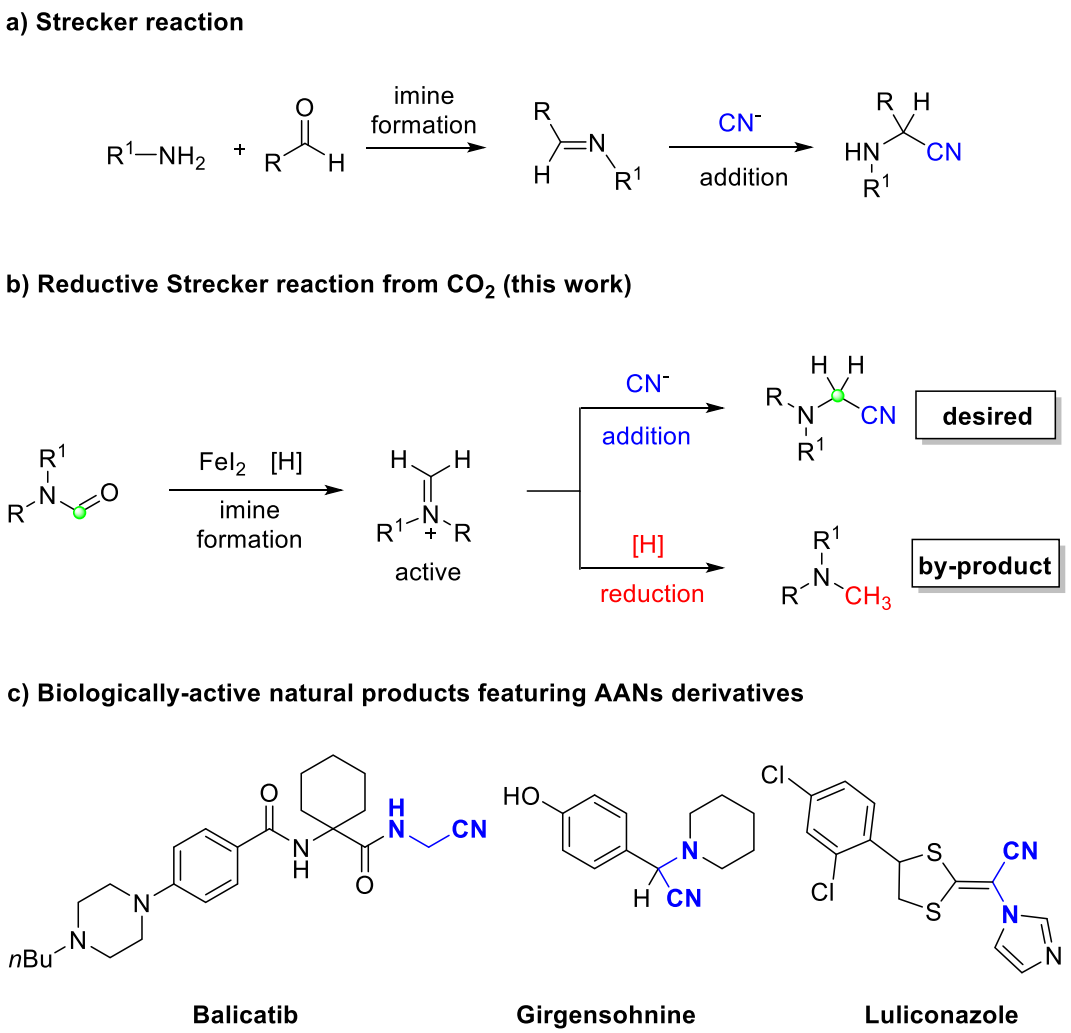


Fig. 1. The choice of CO_2 utilization for AANs intermediates. (a) Strecker reaction. (b) Reductive Strecter reaction from CO_2. (c) Biologically-active natural products featuring AANs derivatives.

amounts of activating agents (eg. Tf_2O/2-F-Py or $[Cp_2ZrHCl]$/TFA). Dixon group [19] and Adolfsson group [20] reported the elegant synthesis of α-amino nitriles from tertiary amides catalyzed by $IrCl(CO)[P(C_6H_5)_3]_2$ (Vaska's catalysts) and $Mo(CO)_6$, respectively. Moreover, Huang and co-workers reported the reductive functionalization of secondary amides catalyzed by $[IrCl(COE)_2]_2$ [21]. *However, in these cases, the efficiency for the reactions of formamides was not explored or rather limited* [19].

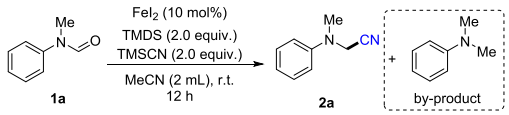
On the other hand, the use of CO_2 as C1 synthon holds promise for sustainable synthesis. Generally employed methods rely largely on the use of organometallic species [22] (Grignard reagents, organoboron, organolithium and organozinc reagents), reductants [23], and unsaturated compounds [24]. These methods exploit the electrophilicity of CO_2 to successfully, prepare alcohols, carboxylic acids and derivatives as well as cyclic compounds [25]. More recently, nucleophilic radical anion CO_2 was generated as key intermediate in photo/electrochemical reductive transformations [26]. Nevertheless, these strategies were mainly based on one-step linear synthesis and only one type of functional group was introduced in the final product. Converting CO_2 into valuable complex molecules is still challenging.

To the best of our knowledge, there is no report on general reductive Strecker cyanation of CO_2-derived formamides to amino acetonitriles. It is well recognized that ligand association and dissociation from metal centers involves significant change in the metal's coordination sphere. As part of our continuing efforts on transition-metal-catalyzed cyanation reactions and CO_2 utilization [27], we describe here FeI_2-catalyzed reductive cyanation of formamides with TMSCN to access AANs products. Using iodide as the ligand showed unexpected substrate reactivity and selectivity for Fe(II)-catalyzed reductive Strecker reaction of formamides.

2. Results and discussion

Aromatic formamides are intermediates in the methanogenesis cycle, involving CO_2 as terminal electron acceptor [28]. Therefore, we have chosen *N*-methylformanilide **1a** as starting material in our initial study to react with TMSCN for reaction condition optimization (Table 1). Reaction optimization considered a variety of parameters such as metal precursors, ligands, reducing agents, additives and solvents. Satisfyingly, we were pleased to find that reductive cyanation of **1a** proceeded to afford 2-(methyl(phenyl)amino)acetonitrile **2a** exclusively in 94% yield at room temperature in the presence of 10 mol% of FeI_2 in MeCN without additional ligands (Table 1, entry 1). FeI_2 catalyst was found essential for good reactivity, and no reaction occurred in the absence of this catalyst (Table 1, entry 2). The Vaska's catalyst [19] and $[RhCl(COD)]_2$ were also tested leading to target product **2a** in lower yields of 49% and 37%, respectively (Table 1, entries 3-4). Significant amounts of

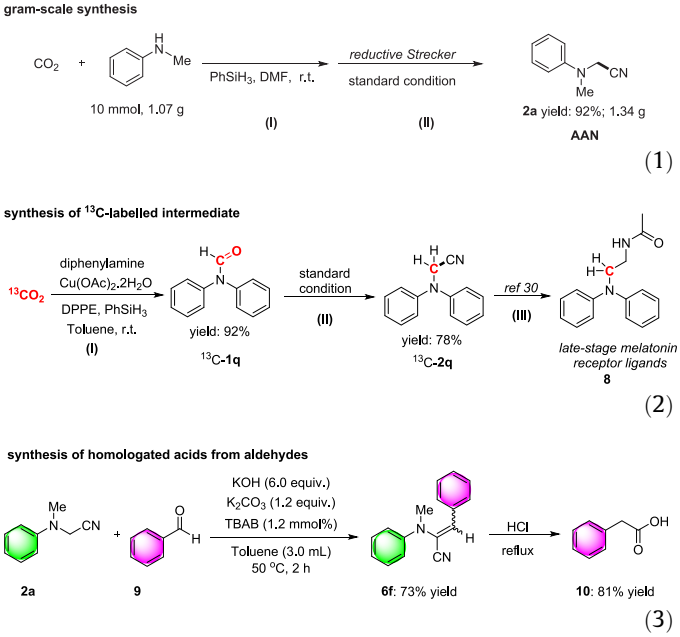
Table 1
Optimization of the reaction conditions.[a]



Entry	Variation of standard conditions	Yield (%)[b]
1	**none**	**94**
2	Without FeI_2	n.r.
3	Vaska's Cata. instead of FeI_2	49 [19]
4	$[RhCl(COD)]_2$ instead of FeI_2	37
5	$Mo(CO)_6$ instead of FeI_2	n.r. [20]
6	$Ni(COD)_2$ instead of FeI_2	n.d.
7	$MnBr(CO)_5$ instead of FeI_2	n.d.
8	CuI instead of FeI_2	n.d.
9	$FeCl_2$ instead of FeI_2	n.d.
10	$FeBr_2$ instead of FeI_2	53
11	$FeBr_2$ and KI instead of FeI_2	91
12	$PhSiH_3$ instead of TMDS	78
13	Toluene instead of MeCN	46
14	DMF instead of MeCN	trace

[a] Reaction conditions: **1a** (0.3 mmol), catalyst (10 mol%), solvent (2.0 mL), additive (10 mol%), N_2, r.t., 12 h.
[b] Isolated yields were shown. n.d. no detected. n.r. no reaction.

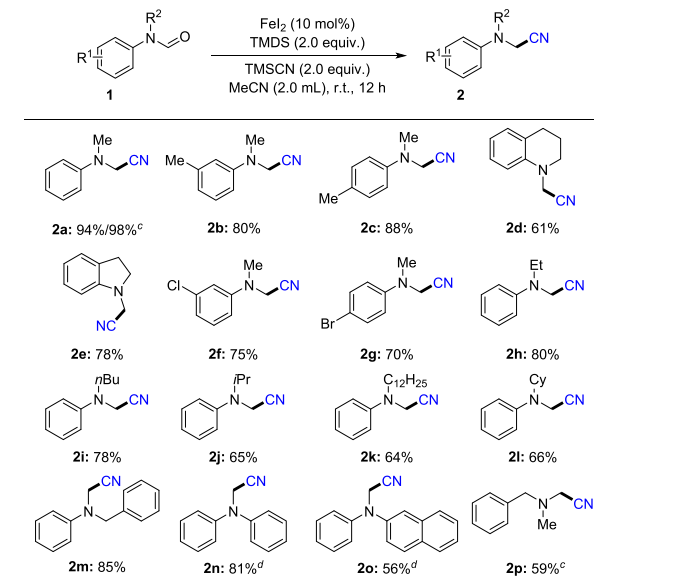
over-reduction product *N*,*N*-dimethylaniline were generated in both cases. Attempts to use other transition metal catalysts such as $Mo(CO)_6$ [20], $Ni(COD)_2$ and $MnBr(CO)_5$ to replace FeI_2 were all unsuccessful (Table 1, entries 5–7). We also investigated a variety of different iron salts in an effort to explore the anion effect, and only analogous $FeBr_2$ resulted in 53% yield of **2a** (Table 1, entries 9–10). In this case, the addition of KI (10 mol%) as iodide source improved the yield significantly (Table 1, entry 11). These results indicate that iodide anion ligand plays an important role in promoting the reaction. The screening of other iodide salts such as CuI was ineffective to generate the desired product **2a**, indicating the crucial role of iron metal center for this transformation (Table 1, entry 8). Exploring other silane reducing agents such as $PhSiH_3$ resulted in lower yields (Table 1, entry 12). Furthermore, solvents screening showed that only MeCN was more suitable solvent compared to toluene or DMF (Table 1, entries 13–14).



With the optimized conditions in hand, we tested the one-pot reaction from CO_2 for the synthesis of amino acetonitrile products. In this case $PhSiH_3$ was used for CO_2 reduction to AAN **2a** in the presence of *N*-Me aniline (Eq. (1)). To our delight, the reaction proceeded smoothly even at gram-scale and 1.34 g of AAN **2a** was obtained at room temperature in high yield (92%) [29]. In addition, this one-pot approach was applied for the synthesis of isotope-labelled melatonin receptor ligand (MLT) intermediate **8** in high yield using ^{13}C-CO_2 (Eq. (2)) [30]. The production of one-carbon homologated carboxylic acids from aldehydes is valuable but only limited methods are known [31]. Using the product of reductive Strecker reaction **2a**, homologated bio-active carboxylic acids **10** or 2-(1-methyl-1H-indol-3-yl)acetic acid were prepared conveniently from benzaldehyde and indole-3-carboxaldehyde in 81% and 86% yields, respectively (Eq. (3)).

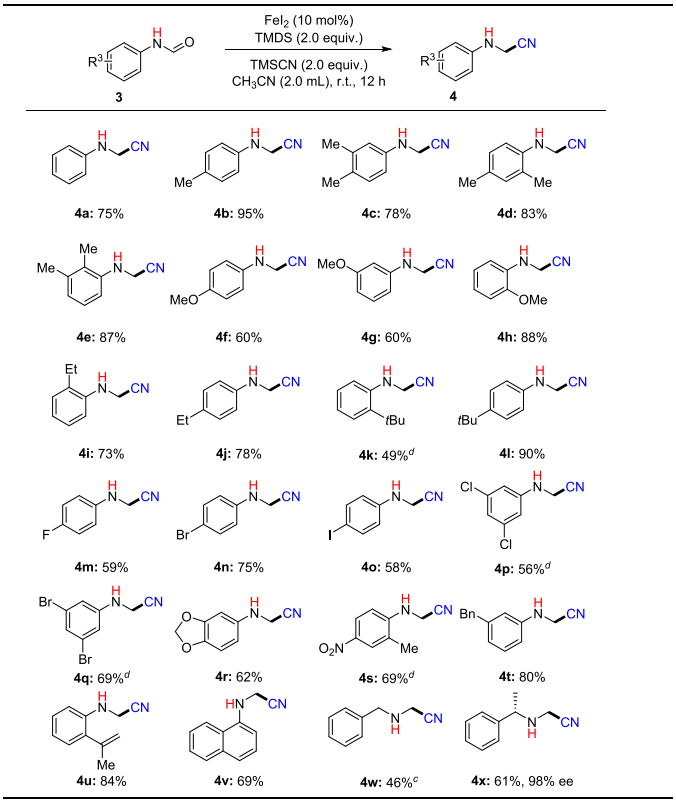
N-Methylformanilide derivatives bearing a methyl group at the *meta* or *para* position converted smoothly under the optimized conditions and afforded the corresponding AANs derivatives in good yields (**2b** and **2c**, 80% and 88%, Table 2). Cyclo-formamides (**1d** and **1e**) were also compatible delivering the desired products in good yields (**2d** and **2e**, 61% and 78%). Notably, the method tolerates substrates bearing halide groups such as chloro and bromo at *meta* or *para* positions (**2f** and **2g**, 70% and 75%), providing the opportunity for further transformations. Furthermore, formamides with various alkyl groups on *N*-atom such as Et, *n*Bu, *i*Pr, $C_{12}H_{25}$ or cyclohexyl groups were examined (**2h**-**2l**) and the reaction afforded the corresponding products in appreciable yields, 64%-80%. Sterically hindered *N*-naphthyl-substituted formanilide were converted smoothly to 2-(naphthalen-2-yl(phenyl)amino)acetonitrile **2o** in 56% yield under elevated temperature of 80 °C. Excellent yields were observed for formamides bearing benzyl or phenyl group (**2m** and **2n**). Moreover, *N*-benzyl-*N*-methylformamide **1p** was also tolerated and the target product **2p** was obtained in 59% yield. These examples show the application potential and substrate tolerance of the method using this iron-catalyzed reductive cyanation strategy. Unfortunately, dialkyl formamides were not

Table 2
Substrate scope of tertiary formamides.[a,b]



[a]Reaction conditions for tertiary amines: substrate **1** (0.3 mmol), TMDS (2.0 equiv.), TMSCN (2.0 equiv.), FeI_2 (10 mol%), MeCN (2 mL), r.t., 12 h.
[b]Yield of isolated product.
[c]Determined by GC, n-dodecane was used as an internal standard.
[d]80 °C, 20 h.

Table 3
Substrate scope of secondary formamides.[a,b]



[a] Reaction conditions for secondary formamides: substrate **3** (0.3 mmol), TMDS (2.0 equiv.), TMSCN (2.0 equiv.), FeI_2 (10 mol%), MeCN (2 mL), r.t., 12 h.
[b] Yield of isolated product.
[c] Determined by GC, *n*-dodecane was used as an internal standard.
[d] 80 °C, 20 h.

suitable substrates and no desired product could be generated (Fig. S4).

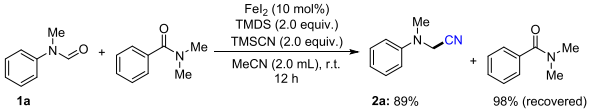
To further investigate the synthetic generality of the reaction, substrate scope was extended to secondary amides to produce AANs derivatives (Table 3). Secondary amino acetonitriles are important building blocks in organic synthesis due to the presence of a synthetically versatile *NH* group. To our delight, the presence of *NH* group tolerated the reaction conditions with the desired products obtained in moderate to good yields. *N*-phenyl formamides bearing methoxy or alkyl groups performed well to deliver the corresponding products **4b**-**4l** in 49–90% yields. Steric effect *ortho* to *N*-H was noticeable and **4k** was obtained in moderate yield. To our satisfaction, electron-deficient substrates were transformed to products **4m**-**4q** smoothly in 58–75% yields. Furthermore, heterocyclic and nitro derivatives were applicable under our reaction conditions affording the corresponding products **4r** and **4s** in 62% and 69%, respectively. Noteworthy, the vinyl moiety remained intact, highlighting the chemoselectivity of this method (**4u**). The 2-(naphthalen-1-ylamino)acetonitrile **4v** was also obtained in good yield and benzylamines were also suitable substrates with the chirality retained in **4x**.

Our approach deployed CO_2 utilization for the construction of valuable molecules is noteworthy. Accordingly, we have demonstrated general synthesis of functionalized compounds *via* reductive Strecker-type cyanation of formamides from CO_2, providing access to amino acetonitriles, olefins, amino ketones, diamines, carboxylic acids and pyrroles *etc*. Specifically, synthetic diversification from **2a**, which could be synthesized at gram-scale, were performed with the results summarized in Fig. 2. The hydrolysis of nitrile group provided the corresponding amide **6a** in 68% yield. *N*-Boc-protected amine **6b** could be obtained by a Ni-catalyzed reduction reaction in 73% yield. Moreover, the nitrile group was hydrolyzed to the carboxylic acid **6c** in high yield. Surprisingly, 2-(methyl(phenyl)amino)-acetonitrile **2a** was selectively converted into 2-(methyl(phenyl)amino)-1-phenylethan-1-one **6d** in 70% yield. The α-cyanoenamines **6f** and **6g** can be conveniently obtained from the reactions with ketones or aldehydes [32]. Moreover, thienyl-substituted acetonitrile **6e** as versatile reagents in electrophilic reactions, nucleophilic and radical reactions, can be gram-scale obtained in 90% yield [33]. Additionally, the reaction of α-cyanoenamines **6f** with methyl isocyanoacetate provided the cyclic product methyl 4-(methyl(phenyl)amino)-3-phenyl-1*H*-pyrrole-2-carboxylate **7** [34].

CO_2 as C1 linker of functional groups, this synthesis strategy based on amino-acetonitrile intermediates involves cleavage of the four C-O bonds in CO_2 and formation of 12 kinds of chemical bonds (including C-H, C—C, C=C, C—O, C=O, C—N, C—S *etc.*) on the same carbon center. Notably, in contrast to traditional methods that are based on the electrophilicity of CO_2, tuning the property of C to a nucleophile was achieved by the Fe-catalyzed selective formation of key amino-acetonitrile intermediates. Beyond the presented synthesis of different types of organic molecules, the newly developed strategy might inspire the utilization of CO_2 as a versatile synthon, and enable the design and synthesis of complex chemicals with the desired functional group on the C atom.

3. Mechanistic studies

To gain insights into the reaction mechanism, NMR measurements and control experiments were conducted. ^{1}H NMR of *N*-methylformanilide interaction with metal iodides showed the peak at 8.057 ppm shifting downfield to 8.133 ppm after addition of KI (10 mol%), which suggests that H-I is engaged in hydrogen bonding interactions (Fig. S1). Additionally, the reaction of *N*-methylformanilide was carried out in the presence of *N*,*N*-dimethylbenzamide. After the reaction, 2-(methyl(phenyl)amino) acetonitrile was detected as the only product accompanied by the recovery of *N*,*N*-dimethylbenzamide (>98%) (Eq. (4)). Next, we moved to intramolecular competing reactions for different type of amide bonds. Gratifyingly, **5a** was obtained in excellent yields with benzamide moiety (**A**) remaining unaltered (Eq. (5)). Therefore, we conclude that *N*-formyl group is crucial for the reaction and the acidic C-H proton probably acts as significant activator (Fig. S2).



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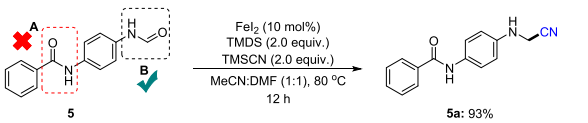

(5)

To understand the high efficiency of FeI_2, we performed the FT-IR and UV–vis measurement for the mixture of FeI_2 and TMSCN. The band at 2080 cm^{-1} was observed (Fig. 3). Considering that $K_4[Fe(CN)_6]$ has the vibrational frequencies at around 2050 cm^{-1} [35]. This result suggests that weaker coordination occurs between FeI_2 and TMSCN compared to ionic Fe^{2+}/CN^- coordination. Using 1:1 mol ratio of FeI_2 and TMSCN, significant amounts of free (or weakly-influenced) TMSCN was still shown in the IR spectrum (1250 cm^{-1}). Besides, weak interaction between FeI_2 and **1a** was

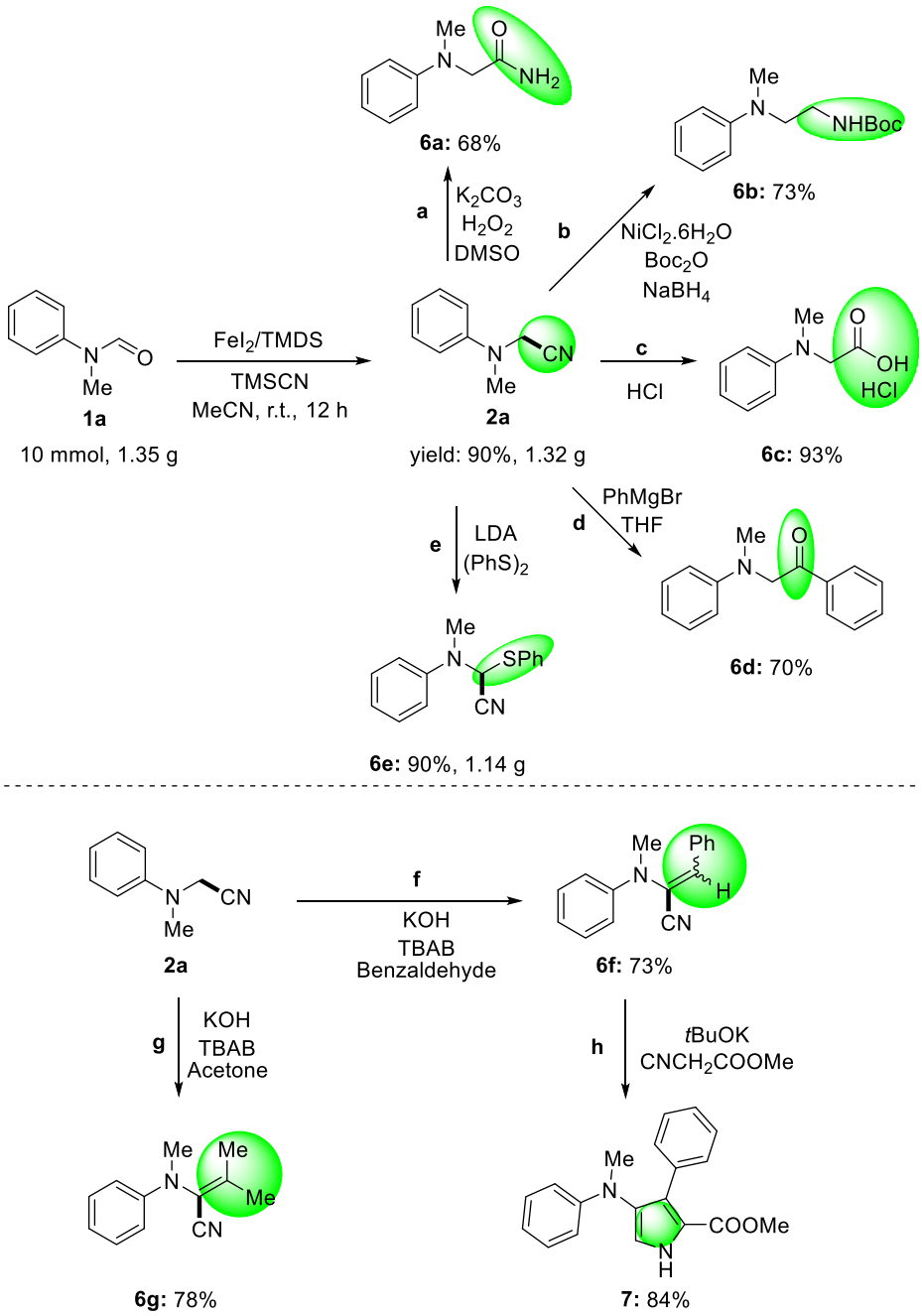

Fig. 2. Synthetic application based on derivatizations of **2a**.

detected with carbonyl group's signal red-shifted by 19.4 cm^{-1} (Fig. S3). In UV–vis spectra, the formation of Fe-I bond was detected when adding KI to the solution of $FeCl_2$ in MeCN. Thus, other than iodide ion, formamide molecules might behave as weak ligands, which allows for a better dissolution of FeI_2 in toluene to give moderate reactivity (Table S1, entry 42; 49% yield).

Based on the above results, we propose the following mechanism for this Fe-catalyzed reductive Stecker reaction (see SI, Scheme 1). The catalyst FeI_2 interacts firstly with the solvent or formamides to dissolve followed by formation of Fe—H species *via* Si—H cleavage [36]. Concerted activation of formamides *via* Fe—O and H—I interactions occurs to have the hydride attack on the carbonyl group. However, the other reaction pathway *via* the formation of α-siloxy nitrile intermediates followed by reduction to generate amino acetonitrile products could not be excluded. Then, the reduced acetal intermediate reacts with CN^- to give the desired product *via* similar concerted activation, with the generation of the Fe-CN type species. The hydridic attack on the carbonyl group of formamides to form the acetal type species, followed by the S_N2 type cyanation reaction to give the desired amino-acetonitrile products. Si—C bond activation might be achieved by the concerted S_N2-type attack of the nucleophilic siloxide ion to Si atom and active species will be regenerated by ligand exchange of cyanide and iodide.

4. Conclusions

In conclusion, we have developed Fe-catalyzed reductive cyanation of formamides to access AANs with excellent chemoselectiv-

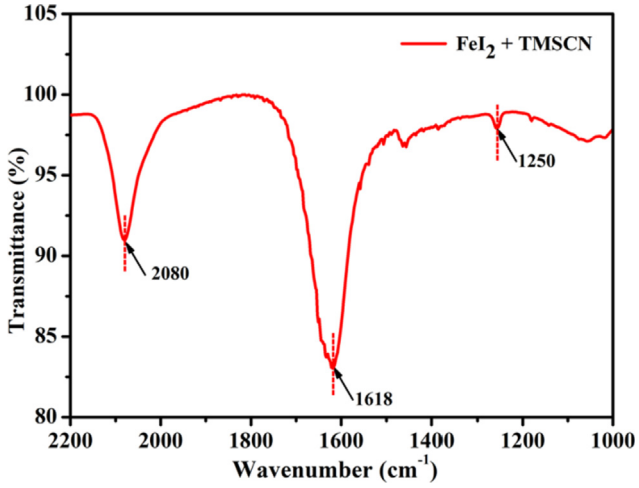

Fig. 3. FT-IR spectra. FeI_2+ TMSCN in DCM for 30 min.

ity. The use of iron (II) iodide as robust catalyst of reductive Strecker reactions to construct AANs derivatives was described for the first time. Notably, a variety of secondary and tertiary formamides were well tolerated in this catalytic system. The applicability of this methodology has been demonstrated by synthesis of ^{13}C-labeled bio-active compounds and gram scale synthesis of AAN involving CO_2. Moreover, the importance of this methodology was confirmed by the many possible transformations of AANs to α-cyanoenamines and phenylsulfanyl acetonitriles. Further investigation of the mechanism and application to other reactions are currently underway.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcat.2021.01.003.

References

[1] For selected reviews on Strecker Reaction, see:
(a) H. Gröger, Catalytic enantioselective Strecker reactions and analogous syntheses, Chem. Rev. 103 (2003) 2795–2828.
(b) J. Wang, X. Liu, X. Feng, Asymmetric Strecker reactions, Chem. Rev. 111 (2011) 6947–6983.
(c) V.V. Kouznetsov, C.E. Puerto Galvis, Strecker reaction and α-amino nitriles: recent advances in their chemistry, synthesis, and biological properties, Tetrahedron 74 (2018) 773–810.
[2] A. Strecker, Ueber die künstliche bildung der Milchsäure und einen neuen, dem Glycocoll homologen Körper, Ann. Chem. Pharm. 75 (1850) 27–45.
[3] D. Papineau, S.J. Mojzsis, J.A. Karhu, B. Martyde, Ammonia from iron (II) reduction of nitrite and the Strecker synthesis: do iron (II) and cyanide interfere with each other, Orig. Life Evol. Biosph. 28 (1998) 1–11.
[4] K.C. Nicolaou, S.A. Snyder, Classics in total synthesis II: more targets, strategies, Wiley-VCH, Weinheim, Germany, 2003.
[5] For selected examples on amino-acetonitriles in organic synthesis, see:
(a) D. Enders, J.P. Shilvock, Recent Applications of α-amino nitrile chemistry, Chem. Soc. Rev. 29 (2000) 359–373.
(b) J.A. González-Vera, M.T. García-López, R. Potential of amino acid-derived α-amino nitriles for generating molecular diversity, R. Herranz, Mini-Rev. Org. Chem. 5 (2008) 209–221.
(c) N. Otto, T. Opatz, Heterocycles from α-aminonitriles, Chem. Eur. J. 20 (2014) 13064–13077.
(d) C. Nájera, J.M. Sansano, Catalytic asymmetric synthesis of α-amino acids, Chem. Rev. 107 (2007) 4584–4671.
(e) S.J. Zuend, M.P. Coughlin, M.P. Lalonde, E.N. Jacobsen, Scaleable catalytic asymmetric Strecker syntheses of unnatural α-amino acids, Nature 461 (2009) 968–970.
[6] L.E. Overman, H. Wild, Preparation of functionalized hydroindol-3-ols via tandem aza-Cope rearrangement-mannich cyclizations. Formal total synthesis of (±)-6a-epipretazettine and related alkaloids, Tetrahedron Lett. 30 (1989) 647–650.
[7] (a) M. Frizler, M. Stirnberg, M.T. Sisay, M. Gütschow, Development of nitrile-based peptidic inhibitors of cysteine cathepsins, Curr. Top. Med. Chem. 10 (2010) 294–322;
(b) L.Y. Vargas Mendez, V.V. Kouznetsov, First girgensohnine analogs prepared through $InCl_3$-catalyzed Strecker reaction and their bioprospection, Curr. Org. Synth. 10 (2013) 969–973;
(c) J. Wijkmans, J. Gossen, Inhibitors of cathepsin K: A patent review (2004–2010), Expert Opin. Ther. Pat. 21 (2011) 1611–1629.
[8] Y. Ping, Q. Ding, Y. Peng, Advances in C-CN bond formation via C-H bond activation, ACS Catal. 6 (2016) 5989–6005.
[9] (a) S.I. Murahashi, N. Komiya, H. Terai, T. Nakae, Aerobic ruthenium-catalyzed oxidative cyanation of tertiary amines with sodium cyanide, J. Am. Chem. Soc. 125 (2003) 15312–15313;
(b) S.I. Murahashi, T. Nakae, H. Terai, N. Komiya, Ruthenium-catalyzed oxidative cyanation of tertiary amines with molecular oxygen or hydrogen peroxide and sodium cyanide: sp^3 C-H bond activation and carbon-carbon bond formation, J. Am. Chem. Soc. 130 (2008) 11005–11012;
(c) S. Verma, S.L. Jain, B. Sain, Acetone ayanohydrin: a convenient alternative of toxic sodium cyanide/acetic acid for oxidative cyanation of tertiary amines, Catal. Lett. 141 (2011) 882–885;
(d) V. Panwar, P. Kumar, S.S. Ray, S.L. Jain, Organic inorganic hybrid cobalt phthalocyanine/polyaniline as efficient catalyst for aerobic oxidation of alcohols in liquid phase, Tetrahedron Lett. 56 (2015) 3948–3953.
[10] (a) W. Han, A.R. Ofial, Iron catalyzed oxidative cyanation of tertiary amines, Chem. Commun. 45 (2009) 5024–5026;
(b) A. Wagner, W. Han, P. Mayer, A.R. Ofial, Iron-catalyzed generation of α-amino nitriles from tertiary amines, Adv. Synth. Catal. 355 (2013) 3058–3070;
(c) L. Zhang, X. Gu, P. Lu, Y. Wang, Synthesis of α-aminonitriles via a $FeSO_4$-mediated oxidative cyanation of tertiary amines with benzoyl cyanide and molecular oxygen or TBHP, Tetrahedron 72 (2016) 2359–2363;
(d) H. Shen, L. Hu, Q. Liu, M.I. Hussain, J. Pan, M. Huang, Y. Xiong, Iron-catalysed sequential reaction towards α-aminonitriles from secondary amines, primary alcohols and trimethylsilyl cyanide, Chem. Commun. 52 (2016) 2776–2779.
[11] S. Singhal, S.L. Jain, B. Sain, An efficient aerobic oxidative cyanation of tertiary amines with sodium cyanide using vanadium based systems as catalysts, Chem. Commun. 45 (2009) 2371–2372.
[12] Y. Zhang, H. Peng, M. Zhang, Y. Cheng, C. Zhu, Gold-complexes catalyzed oxidative α-cyanation of tertiary amines, Chem. Commun. 47 (2011) 2354–2356.
[13] K. Alagiri, K.R. Prabhu, C-H functionalization of tertiary amines by cross dehydrogenative coupling reactions: solvent-free synthesis of α-aminonitriles and β-nitroamines under aerobic condition, Org. Biomol. Chem. 10 (2012) 835–842.
[14] (a) P. Liu, Y. Liu, E.L.-M. Wong, S. Xiang, C.-M. Che, Iron oligopyridine complexes as efficient catalysts for practical oxidation of arenes, alkanes, tertiary amines and N-acyl cyclic amines with oxone, Chem. Sci. 2 (2011) 2187–2195;
(b) P. Kumar, S. Varma, S.L. Jain, A TiO_2 immobilized Ru(II) polyazine complex: a visible-light active photoredox catalyst for oxidative cyanation of tertiary amines, J. Mater. Chem. A 2 (2014) 4514–4519;
(c) V. Panwar, P. Kumar, A. Bansal, S.S. Ray, S.L. Jain, PEGylated magnetic nanoparticles (PEG@Fe_3O_4) as cost effective alternative for oxidative cyanation of tertiary amines via C-H activation, Appl. Catal. A 498 (2015) 25–31;
(d) S. Verma, R.B.N. Baig, C. Han, M.N. Nadagouda, R.S. Varma, Magnetic graphitic carbon nitride: its application in the C-H activation of amines, Chem. Commun. 51 (2015) 15554–15557.
[15] (a) M. Rueping, S. Zhu, R.M. Koenigs, Visible-light photoredox catalyzed oxidative Strecker reaction, Chem. Commun. 47 (2011) 12709–12711;
(b) G. Kumar, P. Solanki, M. Nazish, S. Neogi, R.I. Kureshy, H.K. Noorul, Covalently hooked EOSIN-Y in a Zr(IV) framework as visible-light mediated, heterogeneous photocatalyst for efficient C-H functionalization of tertiary amines, J. Catal. 371 (2019) 298–304.
[16] V. Pace, W. Holzer, B. Olofsson, Increasing the reactivity of amides towards organometallic reagents: an overview, Adv. Synth. Catal. 356 (2014) 3697–3736.
[17] (a) S. Katahara, S. Kobayashi, K. Fujita, T. Matsumoto, T. Sato, N. Chida, An Iridium-catalyzed reductive approach to nitrones from N-hydroxyamides, J. Am. Chem. Soc. 138 (2016) 5246–5249;
(b) M. Nakajima, T. Sato, N. Chida, Iridium-catalyzed chemoselective reductive nucleophilic addition to N-methoxyamides, Org. Lett. 17 (2015) 1696–1699;
(c) M. Yoritate, Y. Takahashi, H. Tajima, C. Ogihara, T. Yokoyama, Y. Soda, T.

Oishi, T. Sato, N. Chida, Unified total synthesis of stemoamide-type alkaloids by chemoselective assembly of five-membered building blocks, J. Am. Chem. Soc. 139 (2017) 18386–18391.
[18] (a) P.-Q. Huang, W. Ou, F. Han, Chemoselective reductive alkynylation of tertiary amides by Ir and Cu(I) bis-metal sequential catalysis, Chem. Commun. 52 (2016) 11967–11970;
(b) H. Chen, J.-L. Ye, P.-Q. Huang, Chemoselective direct reductive trifluoromethylation of amides: a flexible access to functionalized α-trifluoromethylamines, Org. Chem. Front. 5 (2018) 943–947.
[19] (a) Á.L. Fuentes de Arriba, E. Lenci, M. Sonawane, O. Formery, D.J. Dixon, Iridium-catalyzed reductive Strecker reaction for late-stage amide and lactam cyanation, Angew. Chem. Int. Ed. 56 (2017) 3655–3659;
(b) L.-G. Xie, D.J. Dixon, Tertiary amine synthesis via reductive coupling of amides with Grignard reagents, Chem. Sci. 8 (2017) 7492–7497;
(c) A.W. Gregory, A. Chambers, A. Hawkins, P. Jakubec, D.J. Dixon, Iridium-catalyzed reductive nitro-Mannich cyclization, Chem. Eur. J. 21 (2015) 111–114;
(d) P. Gabriel, A.W. Gregory, D.J. Dixon, Iridium-catalyzed aza-spirocyclization of indole-tethered amides: an interrupted pictet-spengler reaction, Org. Lett. 21 (2019) 6658–6662;
(e) L.-G. Xie, J. Rogers, I. Anastasiou, J.A. Leitch, D.J. Dixon, Iridium-catalyzed reductive allylation of esters, Org. Lett. 21 (2019) 6663–6667;
(f) D. Vasu, A.L.F. de Arriba, J.A. Leitch, A. de Gombert, D.J. Dixon, Primary α-tertiary amine synthesis via α-C-H functionalization, Chem. Sci. 10 (2019) 3401–3407.
[20] (a) F. Tinnis, A. Volkov, T. Slagbrand, H. Adolfsson, Chemoselective reduction of tertiary amides under thermal control: formation of either aldehydes or amines, Angew. Chem. Int. Ed. 55 (2016) 4562–4566;
(b) T. Slagbrand, G. Kervefors, F. Tinnis, H. Adolfsson, An efficient one-pot procedure for the direct preparation of 4, 5-dihydroisoxazoles from amides, Adv. Synth. Catal. 359 (2017) 1990–1995;
(c) P. Trillo, T. Slagbrand, F. Tinnis, H. Adolfsson, Facile preparation of pyrimidinediones and thioacrylamides via reductive functionalization of amides, Chem. Commun. 53 (2017) 9159–9162;
(d) P. Trillo, T. Slagbrand, H. Adolfsson, Straightforward α-amino nitrile synthesis through $Mo(CO)_6$-catalyzed reductive functionalization of carboxamides, Angew. Chem. Int. Ed. 57 (2018) 12347–12351.
[21] W. Ou, F. Han, X.-N. Hu, H. Chen, P.-Q. Huang, Iridium-catalyzed reductive alkylations of secondary amides, Angew. Chem. Int. Ed. 130 (2018) 11524–11528.
[22] (a) M.D. Greenhalgh, S.P. Thomas, Iron-catalyzed, highly regioselective synthesis of α-aryl carboxylic acids from styrene derivatives and CO_2, J. Am. Chem. Soc. 134 (2012) 11900–11903;
(b) S. Li, B. Miao, W. Yuan, S. Ma, Carbometalation-carboxylation of 2,3-allenols with carbon dioxide: a dramatic effect of halide anion, Org. Lett. 15 (2013) 977–979;
(c) K. Ukai, M. Aoki, J. Takaya, N. Iwasawa, Rhodium(I)-catalyzed carboxylation of aryl- and alkenylboronic esters with CO_2, J. Am. Chem. Soc. 128 (2006) 8706–8707;
(d) T. Ohishi, M. Nishiura, Z. Hou, Carboxylation of organoboronic esters catalyzed by N-heterocyclic carbene copper(I) complexes, Angew. Chem. Int. Ed. 47 (2008) 5792–5795;
(e) S. Chakraborty, J. Zhang, J.A. Krause, H. Guan, An efficient nickel catalyst for the reduction of carbon dioxide with a borane, J. Am. Chem. Soc. 132 (2010) 8872–8873;
(f) S. Bontemps, L. Vendier, S. Sabo-Etienne, Borane-mediated carbon dioxide reduction at ruthenium: formation of C1 and C2 compounds, Angew. Chem. Int. Ed. 51 (2012) 1671–1674;
(g) K.I. Tominaga, Y. Sasaki, Ruthenium-catalyzed one-pot hydroformylation of alkenes using carbon dioxide as a reactant, J. Mol. Catal. A: Chem. 220 (2004) 159–165;
(h) T. Mita, J. Chen, Y. Sato, Synthesis of arylglycines from CO_2 through α-amino organomanganese species, Org. Lett. 16 (2014) 2200–2203;
(i) V.K. Srivastava, P. Eilbracht, Ruthenium carbonyl-complex catalyzed hydroaminomethylation of olefins with carbon dioxide and amines, Catal. Commun. 10 (2009) 1791–1795;
(j) C.M. Williams, J.B. Johnson, T. Rovis, Nickel-catalyzed reductive carboxylation of styrenes using CO_2, J. Am. Chem. Soc. 130 (2008) 14936–14937;
(k) S. Li, W. Yuan, S. Ma, Highly regio- and stereoselective three-component nickel-catalyzed syn-hydrocarboxylation of alkynes with diethyl zinc and carbon dioxide, Angew. Chem. Int. Ed. 50 (2011) 2578–2582;
(l) C.S. Yeung, V.M. Dong, Beyond Aresta's complex: Ni- and Pd-catalyzed organozinc coupling with CO_2, J. Am. Chem. Soc. 130 (2008) 7826–7827.
[23] (a) T. Fujihara, T. Xu, K. Semba, J. Terao, Y. Tsuji, Copper-catalyzed hydrocarboxylation of alkynes using carbon dioxide and hydrosilanes, Angew. Chem. Int. Ed. 50 (2011) 523–527;
(b) F.J. Fernández-Alvarez, L.A. Oro, Homogeneous catalytic reduction of CO_2 with silicon-hydrides, state of the art, ChemCatChem 10 (2018) 4783–4796.
[24] H. Yoshida, H. Fukushima, J. Ohshita, A. Kunai, CO_2 incorporation reaction using arynes: straightforward access to benzoxazinone, J. Am. Chem. Soc. 128 (2006) 11040–11041.
[25] S. Wang, C. Xi, Recent advances in nucleophile-triggered CO_2-incorporated cyclization leading to heterocycles, Chem. Soc. Rev. 48 (2019) 382–404.
[26] H. Seo, M.H. Katcher, T.F. Jamison, Photoredox activation of carbon dioxide for amino acid synthesis in continuous flow, Nat. Chem. 9 (2017) 453–456.
[27] (a) H. Wang, Y. Dong, C. Zheng, C.A. Sandoval, X. Wang, M. Makha, Y. Li, Catalytic cyanation using CO_2 and NH_3, Chem 4 (2018) 2883–12393;
(b) Y. Wang, L. Fu, H. Qi, S.-W. Chen, Y. Li, Bioinspired synthesis of nitriles from primary amides via zinc/anhydride catalysis, Asian J. Org. Chem. 7 (2018) 367–370;
(c) X. Wang, M. Makha, S.-W. Chen, H. Zheng, Y. Li, $GaCl_3$-catalyzed C-H cyanation of indoles with N-cyanosuccinimide, J. Org. Chem. 84 (2019) 6199–6206;
(d) Z. Huang, X. Jiang, S. Zhou, P. Yang, C. Du, Y. Li, Mn-catalyzed selective double and mono-N-formylation and N-methylation of amines by using CO_2, ChemSusChem 12 (2019) 3054–3059;
(e) Z. Huang, Y. Dong, Y. Li, M. Makha, Y. Li, Enhancing ligand-free Fe-catalyzed aminocarbonylation of alkynes by ZrF_4, ChemCatChem 11 (2019) 5236–5240.
[28] (a) R.K. Thauer, Biochemistry of methanogenesis: a tribute to marjory stephenson, Microbiology 144 (1998) 2377–2406;
(b) N. Shen, S.-J. Zhai, C.W. Cheung, J.-A. Ma, Direct N-formylation of nitroarenes with CO_2, Chem. Commun. 56 (2020) 9620–9623.
[29] H. Lv, Q. Xing, C. Yue, Z. Lei, F. Li, Solvent-promoted catalyst-free *N*-formylation of amines using carbon dioxide under ambient conditions, Chem. Commun. 52 (2016) 6545–6548.
[30] S. Rivara, A. Lodola, M. Mor, A. Bedini, G. Spadoni, V. Lucini, M. Pannacci, F. Fraschini, F. Scaglione, R.O. Sanchez, G. Gobbi, G. Tarzia, *N*-(Substituted-anilinoethyl)amides: design, synthesis, and pharmacological characterization of a new class of melatonin receptor ligands, J. Med. Chem. 50 (2007) 6618–6626.
[31] L.R. Cafiero, T.S. Snowden, General and practical conversion of aldehydes to homologated carboxylic acids, Org. Lett. 10 (2008) 3853–3856.
[32] A. Jończyk, Z. Owczarczyk, Reactions of organic anions. CXXVII. catalytic two-phase (CTP) synthesis of α-cyanoenamines, Synthesis 4 (1986) 297–298.
[33] C.-C. Chen, S.-T. Chen, T.-H. Chuang, J.-M. Fang, 2-(N-methylanilino)-2-phenylsulfanylacetonitrile, a reagent tested for electrophilic, nucleophilic and radical reactions, Chem. Soc. Perkin Trans. 1 (1994) 2217–2221.
[34] J.L. Bullington, R.R. Wolff, P.F. Jackson, Regioselective preparation of 2-Substituted 3, 4-diaryl pyrroles: a concise total synthesis of ningalin b, J. Org. Chem. 67 (2002) 9439–9442.
[35] Y.A. Klyuev, Vibrational spectra of crystalline potassium ferri- and ferrocyanide, J. Appl. Spectrosc. 3 (1965) 30–34.
[36] (a) M.-Y. Hu, P. He, T.-Z. Qiao, W. Sun, W.-T. Li, J. Lian, J.-H. Li, S.-F. Zhu, Iron-catalyzed regiodivergent alkyne hydrosilylation, J. Am. Chem. Soc. 142 (2020) 16894–16902;
(b) M.-Y. Hu, Q. He, S.-J. Fan, Z.-C. Wang, L.-Y. Liu, Y.-J. Mu, Q. Peng, S.-F. Zhu, Ligands with 1,10-phenanthroline scaffold for highly regioselective iron-catalyzed alkene hydrosilylation, Nat. Commun. 9 (2018) 221;
(c) B. Cheng, W. Liu, Z. Lu, Iron-catalyzed highly enantioselective hydrosilylation of unactivated terminal alkenes, J. Am. Chem. Soc. 140 (2018) 5014–5017.